

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

FILE 'SCISEARCH' ENTERED AT 13:59:35 ON 14 AUG 2001
COPYRIGHT (C) 2001 Institute for Scientific Information (ISI) (R)

FILE 'BIOSIS' ENTERED AT 13:59:35 ON 14 AUG 2001
COPYRIGHT (C) 2001 BIOSIS(R)

FILE 'REGISTRY' ENTERED AT 13:59:35 ON 14 AUG 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 American Chemical Society (ACS)

=> s psoralen?

L1 15961 PSORALEN?

=> s l2 and mutagen?

L2 NOT FOUND

The L-number entered could not be found. To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l1 and mutagen?

L2 1137 L1 AND MUTAGEN?

=> s l2 and py<1998

2 FILES SEARCHED...

4 FILES SEARCHED...

5 FILES SEARCHED...

'1998' NOT A VALID FIELD CODE

L3 960 L2 AND PY<1998

=> s l3 and vertebrate

L4 42 L3 AND VERTEBRATE

=> dup rem l4

DUPLICATE IS NOT AVAILABLE IN 'REGISTRY'.

ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L4

L5 42 DUP REM L4 (0 DUPLICATES REMOVED)

=> d ibib ti 1-

YOU HAVE REQUESTED DATA FROM 42 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1997:519395 BIOSIS

DOCUMENT NUMBER: PREV199799818598

TITLE: Processing of targeted **psoralen** cross-links in
Xenopus oocytes.

AUTHOR(S): Segal, David J.; Faruqi, A. Fawad; Glazer, Peter M.;
Carroll, Dana (1)

CORPORATE SOURCE: (1) Dep. Biochemistry, Univ. Utah Sch. Med., Salt Lake
City, UT 84132 USA

SOURCE: Molecular and Cellular Biology, (1997) Vol. 17, No. 11,
PP.

6645-6652.

ISSN: 0270-7306.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Processing of targeted **psoralen** cross-links in Xenopus oocytes.

L5 ANSWER 2 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

search results
for 1st O.A.

09/786,309

filing date 3/12/99

Trying 3106016892...Open

Welcome to STN International! Enter x:x
LOGINID:SSSPTA1635LAN
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 Dec 17 The CA Lexicon available in the CAPLUS and CA files
NEWS 3 Feb 06 Engineering Information Encompass files have new names
NEWS 4 Feb 16 TOXLINE no longer being updated
NEWS 5 Apr 23 Search Derwent WPINDEX by chemical structure
NEWS 6 Apr 23 PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7 May 07 DGENE Reload
NEWS 8 Jun 20 Published patent applications (A1) are now in USPATFULL
NEWS 9 JUL 13 New SDI alert frequency now available in Derwent's
DWPI and DPCI

NEWS EXPRESS July 11 CURRENT WINDOWS VERSION IS V6.0b,
CURRENT MACINTOSH VERSION IS V5.0C (ENG) AND V5.0JB (JP),
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2001
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

All use of STN is subject to the provisions of the STN Customer
agreement. Please note that this agreement limits use to scientific
research. Use for software development or design or implementation
of commercial gateways or other similar uses is prohibited and may
result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 13:59:16 ON 14 AUG 2001

=> file medline embase caplus scisearch biosis reg		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'MEDLINE' ENTERED AT 13:59:35 ON 14 AUG 2001

FILE 'EMBASE' ENTERED AT 13:59:35 ON 14 AUG 2001
COPYRIGHT (C) 2001 Elsevier Science B.V. All rights reserved.

FILE 'CAPLUS' ENTERED AT 13:59:35 ON 14 AUG 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

ACCESSION NUMBER: 1997:214169 BIOSIS
DOCUMENT NUMBER: PREV199799520673
TITLE: Malignant melanoma in patients treated for psoriasis with methoxsalen (**psoralen**) and ultraviolet A radiation (PUVA).
AUTHOR(S): Stern, Robert S. (1); Nichols, Khanh T.; Vakeva, Liisa H.
CORPORATE SOURCE: (1) 330 Brookline Ave., Boston, MA 02215 USA
SOURCE: New England Journal of Medicine, (1997) Vol. 336, No. 15, pp. 1041-1045. *claims 1-5*
ISSN: 0028-4793.
DOCUMENT TYPE: Article
LANGUAGE: English
TI Malignant melanoma in patients treated for psoriasis with methoxsalen (**psoralen**) and ultraviolet A radiation (PUVA).

L5 ANSWER 3 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:126663 BIOSIS
DOCUMENT NUMBER: PREV199799418476
TITLE: Potassium-resistant triple helix formation and improved intracellular gene targeting by oligodeoxyribonucleotides containing 7-deazaxanthine.
AUTHOR(S): Faruqi, A. Fawad; Krawczyk, Stephen H.; Matteucci, Mark D.;
Glazer, Peter M. (1)
CORPORATE SOURCE: (1) Dep. Therapeutic Radiol., Yale Univ. Sch. Med., P.O. Box 208040, New Haven, CT 06520-8040 USA
SOURCE: Nucleic Acids Research, (1997) Vol. 25, No. 3, pp. 633-640.
ISSN: 0305-1048.
DOCUMENT TYPE: Article
LANGUAGE: English
TI Potassium-resistant triple helix formation and improved intracellular gene targeting by oligodeoxyribonucleotides containing 7-deazaxanthine.

L5 ANSWER 4 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:456456 BIOSIS
DOCUMENT NUMBER: PREV199799755659
TITLE: Photogenotoxicity of skin phototumorigenic fluoroquinolone antibiotics detected using the comet assay.
AUTHOR(S): Reavy, Helen J.; Traynor, Nicola J.; Gibbs, Neil K. (1)
CORPORATE SOURCE: (1) Photobiol. Unit, Ninewells Hosp., Dundee DD1 9SY UK
SOURCE: Photochemistry and Photobiology, (1997) Vol. 66, No. 3, pp. 368-373.
ISSN: 0031-8655.
DOCUMENT TYPE: Article
LANGUAGE: English
TI Photogenotoxicity of skin phototumorigenic fluoroquinolone antibiotics detected using the comet assay.

L5 ANSWER 5 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:394418 BIOSIS
DOCUMENT NUMBER: PREV199799693621
TITLE: P53 mutation in squamous cell carcinomas from psoriasis patients treated with **psoralen** plus UVA (PUVA).
AUTHOR(S): Nataraj, Arun J.; Wolf, Peter; Cerroni, Lorenzo; Ananthaswamy, Honnavara N. (1)
CORPORATE SOURCE: (1) Dep. Immunol., Univ. Texas M. D. Anderson Cancer Cent.,

SOURCE: 1515 Holcombe Blvd., Box 178, Houston, TX-77030 USA
Journal of Investigative Dermatology, (1997) Vol. 109, No. 2, pp. 238-243.
ISSN: 0022-202X. *claim 6 & 7*

DOCUMENT TYPE: Article

LANGUAGE: English

TI P53 mutation in squamous cell carcinomas from psoriasis patients treated with **psoralen** plus UVA (PUVA).

L5 ANSWER 6 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1997:303826 BIOSIS

DOCUMENT NUMBER: PREV199799603029

TITLE: Mammalian toxicity of 5-methoxypsoralen and 8-methoxypsoralen, two compounds used in skin photochemotherapy.

AUTHOR(S): Diawara, M. M. (1); Kulkosky, P.; Williams, D. E.; McCrory, S.; Allison, T. G.; Martinez, L. A.

CORPORATE SOURCE: (1) Dep. Biol., Univ. Southern Colorado, Pueblo, CO 81001 USA

SOURCE: Journal of Natural Toxins, (1997) Vol. 6, No. 2, pp. 183-192.
ISSN: 1058-8108.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Mammalian toxicity of 5-methoxypsoralen and 8-methoxypsoralen, two compounds used in skin photochemotherapy.

L5 ANSWER 7 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1997:399787 BIOSIS

DOCUMENT NUMBER: PREV199799698990

TITLE: Photochemical and photobiological studies of a furonaphthopyranone as a benzo-spaced **psoralen** analog in cell-free and cellular DNA.

AUTHOR(S): Adam, Waldemar (1); Mielke, Karsten; Saha-Moeller, Chantou R.; Moeller, Marianne; Stopper, Helga; Hutterer, Rudolf; Schneider, Friedemann W.; Ballmaier, Daniel; Epe, Bernd; Gasparro, Francis F.; Chen, Xinsheng; Kagan, Jacques

CORPORATE SOURCE: (1) Inst. Org. Chem., Univ. Wuerzburg, Am Hubland, D-97074 Wuerzburg Germany

SOURCE: Photochemistry and Photobiology, (1997) Vol. 66, No. 1, pp. 46-54.
ISSN: 0031-8655.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Photochemical and photobiological studies of a furonaphthopyranone as a benzo-spaced **psoralen** analog in cell-free and cellular DNA.

L5 ANSWER 8 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1997:517235 BIOSIS

DOCUMENT NUMBER: PREV199799816438

TITLE: Acute myeloid leukemia following **psoralen** with ultraviolet a therapy: A fluorescence in situ hybridization study.

AUTHOR(S): Kwong, Y. L. (1); Au, W. Y.; Ng, M. H. L.; Chan, L. C.; Au, T. S.

CORPORATE SOURCE: (1) Univ. Dep. Med., Professorial Block, Queen Mary Hosp.,

SOURCE: Pokfulam Rd., Hong Kong Hong Kong
Cancer Genetics and Cytogenetics, (1997) Vol. 99, No. 1,
pp. 11-13.
ISSN: 0165-4608.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Acute myeloid leukemia following **psoralen** with ultraviolet a
therapy: A fluorescence in situ hybridization study.

L5 ANSWER 9 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1997:276827 BIOSIS

DOCUMENT NUMBER: PREV199799576030

TITLE: Gene targeting using triple-helix-forming
oligonucleotides.

AUTHOR(S): Faruqi, A. F.; Wang, G.; Raha, M.; Chan, P.; Seidman, M.
M.; Glazer, P. M. (1)

CORPORATE SOURCE: (1) Dep. Therapeutic Radiol., Yale Univ. Sch. Med., P.O.
Box 208040, 333 Cedar St., New Haven, CT 06520-8040 USA

SOURCE: Felgner, P. L. [Editor]; Heller, M. J. [Editor]; Lehn, P.
[Editor]; Behr, J. P. [Editor]; Szoka, F. C., Jr.
[Editor].

(1996) pp. 47-55. ACS Conference Proceedings Series;
Artificial self-assembling systems for gene delivery.
Publisher: American Chemical Society Marketing Division,
Room 205, 1155 16th St. N.W., Washington, DC 20036, USA.
Meeting Info.: Two Conferences by the Cambridge Healthteck
Institute Wakefield, Massachusetts, USA September 28-29,
1995

ISBN: 0-8412-3415-9.

DOCUMENT TYPE: Book; Conference

LANGUAGE: English

TI Gene targeting using triple-helix-forming oligonucleotides.

L5 ANSWER 10 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:219761 BIOSIS

DOCUMENT NUMBER: PREV199698775890

TITLE: **Mutagenesis** by third-strand-directed
psoralen adducts in repair-deficient human cells:
High frequency and altered spectrum in a xeroderma
pigmentosum variant.

AUTHOR(S): Raha, Manidipa; Wang, Gan; Seidman, Michael M.; Glazer,
Peter M. (1)

CORPORATE SOURCE: (1) Dep. Therapeutic Radiol., Yale Univ. Sch. Med., PO Box
208040, New Haven, CT 06520-8040 USA

SOURCE: Proceedings of the National Academy of Sciences of the
United States of America, (1996) Vol. 93, No. 7, pp.
2941-2946.
ISSN: 0027-8424.

DOCUMENT TYPE: Article

LANGUAGE: English

TI **Mutagenesis** by third-strand-directed **psoralen** adducts
in repair-deficient human cells: High frequency and altered spectrum in a
xeroderma pigmentosum variant.

L5 ANSWER 11 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:283280 BIOSIS

DOCUMENT NUMBER: PREV199699005636

TITLE: Strand specificity of **mutagenic** bypass
replication of DNA containing **psoralen**
monoadducts in a human cell extract.

AUTHOR(S): Thomas, David C.; Svoboda, Daniel L.; Vos, Jean-Michel H.
(1); Kunkel, Thomas A.
CORPORATE SOURCE: (1) UNC Lineberger Comprehensive Cancer Cent., Sch. Med.,
Univ. North Carolina, Chapel Hill, NC 27599-7295 USA
SOURCE: Molecular and Cellular Biology, (1996) Vol. 16, No. 5, pp.
2537-2544.
ISSN: 0270-7306.
DOCUMENT TYPE: Article
LANGUAGE: English
TI Strand specificity of **mutagenic** bypass replication of DNA
containing **psoralen** monoadducts in a human cell extract.

L5 ANSWER 12 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:192982 BIOSIS

DOCUMENT NUMBER: PREV199698749111

TITLE: Angular furoquinolinones, **psoralen** analogs: Novel
antiproliferative agents for skin diseases: Synthesis,
biological activity, mechanism of action, and
computer-aided studies.

AUTHOR(S): Rodighiero, Paolo; Guiotto, Adriano (1); Chilin, Adriana;
Bordin, Franco; Baccichetti, Francarosa; Carlassare,
Francesco; Vedaldi, Daniela; Caffieri, Sergio; Pozzan, A.;
Dall'acqua, Francesco

CORPORATE SOURCE: (1) Dep. Pharmaceutical Sci., Via Fr. Marzolo 5, I-35131
Padova Italy

SOURCE: Journal of Medicinal Chemistry, (1996) Vol. 39, No. 6, pp.
1293-1302.
ISSN: 0022-2623.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Angular furoquinolinones, **psoralen** analogs: Novel
antiproliferative agents for skin diseases: Synthesis, biological
activity, mechanism of action, and computer-aided studies.

L5 ANSWER 13 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:128883 BIOSIS

DOCUMENT NUMBER: PREV199698701018

TITLE: Triplex-mediated, in vitro targeting of **psoralen**
photoadducts within the genome of a transgenic mouse.

AUTHOR(S): Gunther, Edward J.; Havre, Pamela A.; Gasparro, Francis
P.;

Glazer, Peter M. (1)
CORPORATE SOURCE: (1) Dep. Ther. Radiol., Yale Univ. Sch. Med., P.O. Box
208040, 333 Cedar St., New Haven, CT 06520-8040 USA

SOURCE: Photochemistry and Photobiology, (1996) Vol. 63, No. 2,
pp.

207-212.

ISSN: 0031-8655.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Triplex-mediated, in vitro targeting of **psoralen** photoadducts
within the genome of a transgenic mouse.

L5 ANSWER 14 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:447094 BIOSIS

DOCUMENT NUMBER: PREV199699169450

TITLE: The **mutagenic** processing of **psoralen**
photolesions leaves a highly specific signature at an
endogenous human locus.

AUTHOR(S): Laguerbe, A.; Guillouf, C.; Moustacchi, E.; Papadopoulos,
D.

CORPORATE SOURCE: URA 1292, CNRS, Inst. Curie-Biologie, Paris France
SOURCE: Mutation Research, (1996) Vol. 360, No. 3, pp. 205.
Meeting Info.: 25th Annual Meeting of the European
Environmental Mutagen Society Noordwijkerhout, Netherlands
June 18-23, 1995
ISSN: 0027-5107.

DOCUMENT TYPE: Conference

LANGUAGE: English

TI The **mutagenic** processing of **psoralen** photolesions
leaves a highly specific signature at an endogenous human locus.

L5 ANSWER 15 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:510766 BIOSIS

DOCUMENT NUMBER: PREV199598515816

TITLE: Altered repair of targeted **psoralen** photoadducts
in the context of an oligonucleotide-mediated triple
helix.

AUTHOR(S): Wang, Gan; Glazer, Peter M. (1)

CORPORATE SOURCE: (1) Dep. Therapeutic Radiol., Yale Univ. Sch. Med., New
Haven, CT 06520-8040 USA

SOURCE: Journal of Biological Chemistry, (1995) Vol. 270, No. 38,
pp. 22595-22601.
ISSN: 0021-9258.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Altered repair of targeted **psoralen** photoadducts in the context
of an oligonucleotide-mediated triple helix.

L5 ANSWER 16 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:171471 BIOSIS

DOCUMENT NUMBER: PREV199598185771

TITLE: Targeted **mutagenesis** in mammalian cells mediated
by intracellular triple helix formation.

AUTHOR(S): Wang, Gan; Levy, Dan D.; Seidman, Michael M.; Glazer,
Peter

CORPORATE SOURCE: M. (1)
(1) Dep. Therapeutic Radiol, Yale Univ. Sch. Medicine, 333
Cedar St., New Haven, CT 06510 USA

SOURCE: Molecular and Cellular Biology, (1995) Vol. 15, No. 3, pp.
1759-1768.
ISSN: 0270-7306.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Targeted **mutagenesis** in mammalian cells mediated by
intracellular triple helix formation.

L5 ANSWER 17 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:364681 BIOSIS

DOCUMENT NUMBER: PREV199598378981

TITLE: **Mutagenicity** and specific mutation spectrum
induced by 8-methoxypsoralen plus a low dose of UVA in the
hprt gene in diploid human fibroblasts.

AUTHOR(S): Chiou, Chuan-Chian; Yang, Jia-Ling

CORPORATE SOURCE: Inst. Biomedical Sciences, National Tsing Hua Univ.,
Hsinchu 300 Taiwan

SOURCE: Carcinogenesis (Oxford), (1995) Vol. 16, No. 6, pp.
1357-1362.
ISSN: 0143-3334.

DOCUMENT TYPE: Article

LANGUAGE: English

TI **Mutagenicity** and specific mutation spectrum induced by
8-methoxypsoralen plus a low dose of UVA in the hprt gene in diploid
human
fibroblasts.

L5 ANSWER 18 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:208636 BIOSIS

DOCUMENT NUMBER: PREV199598222936

TITLE: **Mutagenesis** by 8-methoxypsoralen and
5-methylangelicin photoadducts in mouse fibroblasts:
Mutations at cross-linkable sites induced by monoadducts
as

AUTHOR(S): Gunther, Edward J.; Yeasky, Toni M.; Gasparro, Francis P.;
Glazer, Peter M. (1)

CORPORATE SOURCE: (1) Dep. Therapeutic Radiol., Yale Univ. Sch. Med., P.O.
Box 208040, New Haven, CT 06520-8040 USA

SOURCE: Cancer Research, (1995) Vol. 55, No. 6, pp. 1283-1288.
ISSN: 0008-5472.

DOCUMENT TYPE: Article

LANGUAGE: English

TI **Mutagenesis** by 8-methoxypsoralen and 5-methylangelicin
photoadducts in mouse fibroblasts: Mutations at cross-linkable sites
induced by monoadducts as well as cross-links.

L5 ANSWER 19 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:528383 BIOSIS

DOCUMENT NUMBER: PREV199598542683

TITLE: Elimination of potential **mutagenicity** in platelet
concentrates that are virally inactivated with
psoralens and ultraviolet A light.

AUTHOR(S): Margolis-Nunno, H. (1); Robinson, R.; Ben-Hur, E.; Chin,
S.; Orme, T.; Horowitz, B.

CORPORATE SOURCE: (1) Lindsley F. Kimball Res. Inst., N.Y. Blood Cent., 310
E. 67th St., New York, NY 10021 USA

SOURCE: Transfusion (Bethesda), (1995) Vol. 35, No. 10, pp.
855-862.
ISSN: 0041-1132.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Elimination of potential **mutagenicity** in platelet concentrates
that are virally inactivated with **psoralens** and ultraviolet A
light.

L5 ANSWER 20 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:279525 BIOSIS

DOCUMENT NUMBER: PREV199598293825

TITLE: Targeted **mutagenesis** in mammalian cells mediated
by intracellular triple helix formation: A new approach to
gene therapy.

AUTHOR(S): Wang, Gan (1); Levy, Dan D.; Seidman, Michael M.; Glazer,
Peter M. (1)

CORPORATE SOURCE: (1) Dep. Ther. Radiol., Yale Univ. Sch. Med., 333 Cedar
St., New Haven, CT 06510 USA

SOURCE: Journal of Cellular Biochemistry Supplement, (1995) Vol.
0,

No. 21A, pp. 386.

Meeting Info.: Keystone Symposium on Gene Therapy and
Molecular Medicine Steamboat Springs, Colorado, USA March
26-April 1, 1995

ISSN: 0733-1959.

DOCUMENT TYPE: Conference

LANGUAGE: English

TI Targeted **mutagenesis** in mammalian cells mediated by intracellular triple helix formation: A new approach to gene therapy.

L5 ANSWER 21 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:510998 BIOSIS

DOCUMENT NUMBER: PREV199598516048

TITLE: Triple helix directed **psoralen** adducts induce a low frequency of recombination in an SV40 shuttle vector.

AUTHOR(S): Sandor, Zoltan (1); Bredberg, Anders

CORPORATE SOURCE: (1) Dep. Med. Microbiol., Univ. Lund, General Hosp., S-214 01 Malmo Sweden

SOURCE: Biochimica et Biophysica Acta, (1995) Vol. 1263, No. 3, pp. 235-240.

ISSN: 0006-3002.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Triple helix directed **psoralen** adducts induce a low frequency of recombination in an SV40 shuttle vector.

L5 ANSWER 22 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:266712 BIOSIS

DOCUMENT NUMBER: PREV199598281012

TITLE: Genotoxic potential of **psoralen** cross-links versus monoadducts in normal human lymphoblasts.

AUTHOR(S): Laquerbe, A. (1); Moustacchi, E.; Papadopoulo, D.

CORPORATE SOURCE: (1) Inst. Curie-Biologie, URA 1292 CNRS, 26 rue d'Ulm, 75231 Paris, Cedex 05 France

SOURCE: Mutation Research, (1995) Vol. 346, No. 3, pp. 173-179.

ISSN: 0027-5107.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Genotoxic potential of **psoralen** cross-links versus monoadducts in normal human lymphoblasts.

L5 ANSWER 23 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:331601 BIOSIS

DOCUMENT NUMBER: PREV199598345901

TITLE: **Mutagenesis** in mammalian cells by 8-methoxypsoralen, 5-methylangelicin, and **psoralen**-conjugated triplex-forming oligonucleotides.

AUTHOR(S): Glazer, P. M. (1); Gasparro, F. P.; Wang, G.; Gunther, E. J.

CORPORATE SOURCE: (1) Dep. Therapeutic Radiol., Yale Sch. Med., P.O. Box 208040, New Haven, CT 06520 USA

SOURCE: Photochemistry and Photobiology, (1995) Vol. 61, No. 5 SUPPL., pp. 84S.

Meeting Info.: 23rd Annual Meeting of the American Society for Photobiology Washington, D.C., USA June 17-22, 1995

ISSN: 0031-8655.

DOCUMENT TYPE: Conference

LANGUAGE: English

TI **Mutagenesis** in mammalian cells by 8-methoxypsoralen, 5-methylangelicin, and **psoralen**-conjugated triplex-forming oligonucleotides.

L5 ANSWER 24 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:21338 BIOSIS
DOCUMENT NUMBER: PREV199698593473
TITLE: The **mutagenic** progressing of **psoralen**
photolesions leaves a highly specific signature at an
endogenous human locus.
AUTHOR(S): Laquerbe, Agnes; Guillouf, Christel; Moustacchi, Ethel;
Papadopoulo, Dora (1)
CORPORATE SOURCE: (1) URA 1292 du CNRS, Inst. Curie Section Recherche, 26
rue
d'Ulm, 75231 Paris, Cedex 05 France
SOURCE: Journal of Molecular Biology, (1995) Vol. 254, No. 1, pp.
38-49.
ISSN: 0022-2836.
DOCUMENT TYPE: Article
LANGUAGE: English
TI The **mutagenic** progressing of **psoralen** photolesions
leaves a highly specific signature at an endogenous human locus.

L5 ANSWER 25 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1994:390592 BIOSIS
DOCUMENT NUMBER: PREV199497403592
TITLE: Repair of triple helix directed **psoralen** adducts
in human cells.
AUTHOR(S): Sandor, Zoltan (1); Bredberg, Anders
CORPORATE SOURCE: (1) Dep. Med. Microbiol., Lund Univ., General Hosp., S-214
01 Malmo Sweden
SOURCE: Nucleic Acids Research, (1994) Vol. 22, No. 11, pp.
2051-2056.
ISSN: 0305-1048.
DOCUMENT TYPE: Article
LANGUAGE: English
TI Repair of triple helix directed **psoralen** adducts in human cells.

L5 ANSWER 26 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1995:34453 BIOSIS
DOCUMENT NUMBER: PREV199598048753
TITLE: DNA damage and topoisomerase II inhibition induced by a
benzopsoralen derivative.
AUTHOR(S): Pani, B.; Barbisin, M.; Russo, E. (1); Tamaro, M.;
Baccichetti, F.; Carlassare, F.; Marzano, C.; Rodighiero,
P.; Bordin, F.
CORPORATE SOURCE: (1) Dip. de Biochim., Biosfisica e Chimica delle
Macromol.,
Univ. di Trieste, Via Giorgieri 1, I-34127 Trieste Italy
SOURCE: Mutation Research, (1994) Vol. 311, No. 2, pp. 277-285.
ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English
TI DNA damage and topoisomerase II inhibition induced by a benzopsoralen
derivative.

L5 ANSWER 27 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1994:162525 BIOSIS
DOCUMENT NUMBER: PREV199497175525
TITLE: Mutation specificity of 8-methoxypsoralen plus two does of
UVA irradiation in the hprt gene in diploid human
fibroblasts.
AUTHOR(S): Yang, Shih-Ching; Lin, Jin-Guo; Chiou, Chiuan-Chian; Chen,
Lin-Yi; Yang, Jia-Ling
CORPORATE SOURCE: Inst. Biomedical Sci., Natl. Tsing Hua Univ., Hsinchu 300

Taiwan
SOURCE: Carcinogenesis (Oxford), (1994) Vol. 15, No. 2, pp.
201-207.
ISSN: 0143-3334.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Mutation specificity of 8-methoxypsoralen plus two doses of UVA
irradiation
in the hprt gene in diploid human fibroblasts.

L5 ANSWER 28 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1994:230968 BIOSIS

DOCUMENT NUMBER: PREV199497243968

TITLE: The study on the effects of **psoralen** derivatives
on epidermal melanocytes in C57BL mice after topical
photochemotherapy.

AUTHOR(S): Lee, Seung Min (1); Hann, Seung Kyung; Park, Yoon Kee

CORPORATE SOURCE: (1) Dep. Dermatol., Yonsei Univ. Coll. Med., Seoul South
Korea

SOURCE: Annals of Dermatology, (1994) Vol. 6, No. 1, pp. 1-8.

ISSN: 1013-9087.

DOCUMENT TYPE: Article

LANGUAGE: English

TI The study on the effects of **psoralen** derivatives on epidermal
melanocytes in C57BL mice after topical photochemotherapy.

L5 ANSWER 29 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1994:17004 BIOSIS

DOCUMENT NUMBER: PREV199497030004

TITLE: Targeted **mutagenesis** of simian virus 40 DNA
mediated by a triple helix-forming oligonucleotide.

AUTHOR(S): Havre, Pamela A.; Glazer, Peter M. (1)

CORPORATE SOURCE: (1) Dep. Therapeutic Radiol., Yale Univ. Sch. Med., 333
Cedar St., New Haven, CN 06510 USA

SOURCE: Journal of Virology, (1993) Vol. 67, No. 12, pp.
7324-7331.

ISSN: 0022-538X.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Targeted **mutagenesis** of simian virus 40 DNA mediated by a triple
helix-forming oligonucleotide.

L5 ANSWER 30 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1993:411625 BIOSIS

DOCUMENT NUMBER: PREV199396077350

TITLE: UV-induced mutations in a shuttle vector replicated in
repair deficient trichothiodystrophy cells differ with
those in genetically-related cancer prone xeroderma
pigmentosum.

AUTHOR(S): Madzak, Catherine; Armier, Jacques; Stary, Anne;

Daya-Grosjean, Leela; Sarasin, Alain (1)

CORPORATE SOURCE: (1) Lab. Molecular Genet., Inst. Recherches Scientifiques
Cancer, BP n 8, 94801 Villejuif Cedex France

SOURCE: Carcinogenesis (Oxford), (1993) Vol. 14, No. 7, pp.
1255-1260.

ISSN: 0143-3334.

DOCUMENT TYPE: Article

LANGUAGE: English

TI UV-induced mutations in a shuttle vector replicated in repair deficient
trichothiodystrophy cells differ with those in genetically-related cancer

prone xeroderma pigmentosum.

L5 ANSWER 31 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1993:394723 BIOSIS

DOCUMENT NUMBER: PREV199396070023

TITLE: Determination of residual 4'-aminomethyl-4,5',8-trimethylpsoralen and **mutagenicity** testing following **psoralen** plus UVA treatment of platelet suspensions.

AUTHOR(S): Wagner, Stephen J. (1); White, Randy; Wolf, Ludwig; Chapman, John; Robinette, Daniel; Lawlor, Timothy E.; Dodd,

CORPORATE SOURCE: Roger Y.
(1) American Red Cross Blood Serv., Jerome H. Holland Lab. Biomed. Sci., 15601 Crabbs Branch Way, Rockville, MD 29855 USA

SOURCE: Photochemistry and Photobiology, (1993) Vol. 57, No. 5, pp. 819-824.

ISSN: 0031-8655.

DOCUMENT TYPE: Article

LANGUAGE: English

TI Determination of residual 4'-aminomethyl-4,5',8-trimethylpsoralen and **mutagenicity** testing following **psoralen** plus UVA treatment of platelet suspensions.

claim 2

L5 ANSWER 32 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1994:94447 BIOSIS

DOCUMENT NUMBER: PREV199497107447

TITLE: Novel **psoralens** with enhanced UVA dependent inactivation of human immunodeficiency virus and reduced **mutagenicity** in the absence of UVA light.

AUTHOR(S): Wollowitz, S. (1); Fang, Y.; Jiatao, P.; Nerio, A.; Spielmann, H. P.; Lin, L.; Behrman, B.; Londe, H.; Alfonso,

R.; Corash, L.; Isaacs, S.

CORPORATE SOURCE: (1) Steritech Inc., Concord, CA USA

SOURCE: Blood, (1993) Vol. 82, No. 10 SUPPL. 1, pp. 402A.
Meeting Info.: Thirty-fifth Annual Meeting of the American Society of Hematology St. Louis, Missouri, USA December 3-7, 1993

ISSN: 0006-4971.

DOCUMENT TYPE: Conference

LANGUAGE: English

TI Novel **psoralens** with enhanced UVA dependent inactivation of human immunodeficiency virus and reduced **mutagenicity** in the absence of UVA light.

L5 ANSWER 33 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1993:206881 BIOSIS

DOCUMENT NUMBER: PREV199395108106

TITLE: 8-Methoxypsoralen induced mutations are highly targeted at crosslinkable sites of photoaddition on the

non-transcribed

strand of a mammalian chromosomal gene.

AUTHOR(S): Sage, E.; Drobetsky, E. A.; Moustacchi, E.

CORPORATE SOURCE: CNRS URA 1292, Inst. Curie-Section de Biologie, 26 rue d'Ulm, 75231 Paris Cedex 05 France

SOURCE: EMBO (European Molecular Biology Organization) Journal, (1993) Vol. 12, No. 2, pp. 397-402.

ISSN: 0261-4189.
DOCUMENT TYPE: Article
LANGUAGE: English
TI 8-Methoxypsoralen induced mutations are highly targeted at crosslinkable sites of photoaddition on the non-transcribed strand of a mammalian chromosomal gene.

L5 ANSWER 34 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:461750 BIOSIS
DOCUMENT NUMBER: PREV199396106650
TITLE: **Mutagenic processing of psoralen**
monoadducts differ in normal and Fanconi anemia cells.
AUTHOR(S): Guillouf, Christel; Laquerbe, Agnes; Moustacchi, Ethel;
Papadopoulos, Dora
CORPORATE SOURCE: Inst. Curie, Sect. Biol., URA 1292 CNRS, 26 rue d'Ulm,
75231 Paris Cedex 05 France
SOURCE: Mutagenesis, (1993) Vol. 8, No. 4, pp. 355-361.
ISSN: 0267-8357.
DOCUMENT TYPE: Article
LANGUAGE: English
TI **Mutagenic processing of psoralen** monoadducts differ in
normal and Fanconi anemia cells.

L5 ANSWER 35 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:349514 BIOSIS
DOCUMENT NUMBER: PREV199396046514
TITLE: Phototoxic coumarins in limes.
AUTHOR(S): Nigg, H. N. (1); Nordby, H. E.; Beier, R. C.; Dillman, A.;
Macias, C.; Hansen, R. C.
CORPORATE SOURCE: (1) Citrus Res. Education Center, Univ. Fla., IFAS, 700
Experiment Station Road, Lake Alfred, FL 33850 USA
SOURCE: Food and Chemical Toxicology, (1993) Vol. 31, No. 5, pp.
331-335.
ISSN: 0278-6915.
DOCUMENT TYPE: Article
LANGUAGE: English
TI Phototoxic coumarins in limes.

L5 ANSWER 36 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:281594 BIOSIS
DOCUMENT NUMBER: PREV199396011819
TITLE: **Psoralen** photochemotherapy (PUVA) and pregnancy.
AUTHOR(S): Gunnarskog, Jan G.; Kallen, A. J. Bengt; Lindelof, Bernt
G.; Sigurgeirsson, Bardur
CORPORATE SOURCE: Dep. Dermatology, Karolinska Hosp., S-104 01 Stockholm
Sweden
SOURCE: Archives of Dermatology, (1993) Vol. 129, No. 3, pp.
320-323.
ISSN: 0003-987X.
DOCUMENT TYPE: Article
LANGUAGE: English
TI **Psoralen** photochemotherapy (PUVA) and pregnancy.

L5 ANSWER 37 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:432641 BIOSIS
DOCUMENT NUMBER: PREV199396087266
TITLE: Molecular spectrum of mutations induced at the HPRT locus
by a cross-linking agent in human cell lines with
different
repair capacities.

AUTHOR(S): Papadopulo, D. (1); Laquerbe, A.; Guillouf, C.;
Moustacchi, E.
CORPORATE SOURCE: (1) Inst. Curie - Biol., 26 rue d'Ulm, 75231 Paris Cedex
05 France
SOURCE: Mutation Research, (1993) Vol. 294, No. 2, pp. 167-177.
ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English
TI Molecular spectrum of mutations induced at the HPRT locus by a
cross-linking agent in human cell lines with different repair
capacities.

L5 ANSWER 38 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:432642 BIOSIS
DOCUMENT NUMBER: PREV199396087267
TITLE: Cytogenetic evidence for differences in DNA incision
activity in xeroderma pigmentosum group A, C and D cells
after X-irradiation during G-2 phase.
AUTHOR(S): Parshad, R. (1); Tarone, R. E.; Price, F. M.; Sanford, K.
K.
CORPORATE SOURCE: (1) Lab. Cell. Mol. Biol., Natl. Cancer Inst., Bethesda,
MD 20892 USA
SOURCE: Mutation Research, (1993) Vol. 294, No. 2, pp. 149-155.
ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English
TI Cytogenetic evidence for differences in DNA incision activity in
xeroderma pigmentosum group A, C and D cells after X-irradiation during G-2 phase.

L5 ANSWER 39 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:235194 BIOSIS
DOCUMENT NUMBER: PREV199395126369
TITLE: **Mutagenic** and antimutagenic activities of Uncaria
tomentosa and its extracts.
AUTHOR(S): Rizzi, Renato; Re, Francesco; Bianchi, Antonio; De Feo,
Vincenzo (1); De Simone, Francesco; Bianchi, Livia;
Stivala, Lucia Anna
CORPORATE SOURCE: (1) Dip. Chim. delle Sostanze Naturali, Univ. degli Studi
'Federico II', Via Domenico Montesano 49, 80131 Napoli
Italy
SOURCE: Journal of Ethnopharmacology, (1993) Vol. 38, No. 1, pp.
63-77.
ISSN: 0378-8741.
DOCUMENT TYPE: Article
LANGUAGE: English
TI **Mutagenic** and antimutagenic activities of Uncaria tomentosa and
its extracts.

L5 ANSWER 40 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:415533 BIOSIS
DOCUMENT NUMBER: PREV199396081258
TITLE: A critical review of the genotoxic potential of electric
and magnetic fields.
AUTHOR(S): McCann, Joyce (1); Dietrich, Fred; Rafferty, Charles;
Martin, Alice O.
CORPORATE SOURCE: (1) ICF Kaiser Engineers Inc., 1800 Harrison Street, 7th

SOURCE: Floor, Oakland, CA 94612 USA
Mutation Research, (1993) Vol. 297, No. 1, pp. 61-95.
ISSN: 0027-5107.

DOCUMENT TYPE: Article

LANGUAGE: English

TI A critical review of the genotoxic potential of electric and magnetic fields.

L5 ANSWER 41 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1993:286820 BIOSIS

DOCUMENT NUMBER: PREV199345004945

TITLE: **Mutagenic** processing of **psoralen**
monoadducts differ in normal and Fanconi anemia cells.

AUTHOR(S): Guillouf, C.; Papadopoulo, D.; Laquerbe, A.; Moustacchi, E.

CORPORATE SOURCE: Inst. Curie Biol., Paris France

SOURCE: Environmental and Molecular Mutagenesis, (1993) Vol. 21,
No. SUPPL. 22, pp. 26.
Meeting Info.: 24th Annual Scientific Meeting of the
Environmental Mutagen Society Norfolk, Virginia, USA April
17-22, 1993
ISSN: 0893-6692.

DOCUMENT TYPE: Conference

LANGUAGE: English

TI **Mutagenic** processing of **psoralen** monoadducts differ in
normal and Fanconi anemia cells.

L5 ANSWER 42 OF 42 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1993:121862 BIOSIS

DOCUMENT NUMBER: PREV199395065962

TITLE: Photobiological activity of certain new
methylazapsoralens.

AUTHOR(S): Baccichetti, Francarosa; Bordin, Franco (1); Simonato,
Morena; Toniolo, Luana; Marzano, Christine; Rodighiero,
Paolo; Chilin, Adriana; Carllassare, Francesco

CORPORATE SOURCE: (1) Dep. Pharmaceutical Sciences, Padua University: Centre
di Studio Sulla Chimica Del Farmaco e Del Prodotti,
Biologicamente Attivi, C.N.R., Via Marzolo 5, 35131 Padova
Italy

SOURCE: Farmaco (Rome), (1992) Vol. 47, No. 12, pp. 1529-1541.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English; Italian

TI Photobiological activity of certain new methylazapsoralens.

=> d history

(FILE 'HOME' ENTERED AT 13:59:16 ON 14 AUG 2001)

FILE 'MEDLINE, EMBASE, CAPLUS, SCISEARCH, BIOSIS, REGISTRY' ENTERED AT
13:59:35 ON 14 AUG 2001

L1 15961 S PSORALEN?
L2 1137 S L1 AND MUTAGEN?
L3 960 S L2 AND PY<1998
L4 42 S L3 AND VERTEBRATE
L5 42 DUP REM L4 (0 DUPLICATES REMOVED)

=> s 12 and animal

L6 272 L2 AND ANIMAL

=> s 16 and py<1998
2 FILES SEARCHED...
4 FILES SEARCHED...
5 FILES SEARCHED...
'1998' NOT A VALID FIELD CODE
L7 219 L6 AND PY<1998

=> s 17 and trimethyl?
L8 45 L7 AND TRIMETHYL?

=> dup rem 18
DUPLICATE IS NOT AVAILABLE IN 'REGISTRY'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L8
L9 35 DUP REM L8 (10 DUPLICATES REMOVED)

=> d 19 ibib abs 1-
YOU HAVE REQUESTED DATA FROM 35 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:121398 CAPLUS
DOCUMENT NUMBER: 126:127852
TITLE: Triple helix-forming oligonucleotide conjugates with
mutagens for induction of site-specific
recombination
INVENTOR(S): Glazer, Peter M.; Lin, L. Michael; George, Jay
PATENT ASSIGNEE(S): Yale University, USA; Oncorphan, Inc.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9641008	A1	19961219	WO 1996-US9424	19960606 <--
W: AU, BR, CA, CN, CZ, FI, HU, IL, JP, KP, KR, MX, NO, NZ, SG, SK, UA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,				
SE				
US 5776744	A	19980707	US 1995-467126	19950607
AU 9660995	A1	19961230	AU 1996-60995	19960606 <--
EP 871771	A1	19981021	EP 1996-918306	19960606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1995-467126	19950607
			WO 1996-US9424	19960606

AB A method of inducing homologous recombination by site-specific induction
of DNA damage is described. The method uses two introduced DNAs: one is
a

mutagen-linked single-stranded oligonucleotide capable of
specifically binding to double-stranded DNA to form a triple-stranded
helix, and the second is a donor DNA fragment capable of undergoing
homologous recombination with DNA targeted by the oligonucleotide. The
oligonucleotide brings the **mutagenic** moiety to the desired site
and the damage caused by the **mutagen** stimulates DNA repair with
the formation of recombinogenic free ends. The method is demonstrated by
using **psoralen** conjugates to induce recombination of the supF

gene in COS cells. A recombination frequency with viral donor DNA of 36.3% was obsd.

L9 ANSWER 2 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:283280 BIOSIS
DOCUMENT NUMBER: PREV199699005636
TITLE: Strand specificity of **mutagenic** bypass
replication of DNA containing **psoralen**
monoadducts in a human cell extract.
AUTHOR(S): Thomas, David C.; Svoboda, Daniel L.; Vos, Jean-Michel H.
(1); Kunkel, Thomas A.
CORPORATE SOURCE: (1) UNC Lineberger Comprehensive Cancer Cent., Sch. Med.,
Univ. North Carolina, Chapel Hill, NC 27599-7295 USA
SOURCE: Molecular and Cellular Biology, (1996) Vol. 16, No. 5, pp.
2537-2544.
ISSN: 0270-7306.
DOCUMENT TYPE: Article *claim 2*
LANGUAGE: English

AB **Psoralens** are **mutagenic** compounds of vegetable origin that are used as photosensitizing agents in the treatment of various skin diseases, blood cell cancer, and autoimmune disorders. To study the mechanism of **mutagenicity** of **psoralens** in humans, we examined the efficiency and fidelity of simian virus 40 origin-dependent replication in a human cell extract of M13mp2 DNA randomly treated with the **psoralen** derivative 4'-hydroxymethyl-4,5',8-trimethyl **psoralen** plus UVA irradiation. Replication of DNA treated with variable amounts of 4'-hydroxymethyl-4,5',8-trimethyl **psoralen** and a fixed UVA fluence was inhibited in a concentration-dependent manner. However, covalently closed monomer-length circular replication products were observed. Product analysis by renaturing agarose gel electrophoresis after cross-linking with 250- to 280-nm UV light indicated that approximately 1 of 9 **psoralen** monoadducts was bypassed during in vitro replication. Introduction of product DNA into Escherichia coli to score replication errors in the lacZ-alpha reporter gene demonstrated that replication of the damaged DNA was more **mutagenic** than was replication of undamaged DNA. Sequence analysis of lacZ mutants revealed that damage-dependent replication errors were predominantly T cntdot A fwdarw

C cntdot G transitions, transversions at C cntdot G base pairs, and deletions of single A cntdot T base pairs, the last occurring most frequently in homopolymeric runs. A comparison of error specificities with two substrates having the replication origin asymmetrically placed on opposite sides of the mutational target suggests that the lagging-strand replication apparatus is less accurate than the leading-strand replication apparatus for **psoralen** monoadduct-dependent deletion errors. A model is proposed based on the preferential loopout of the monoadducted base from the strand that templates retrograde discontinuous synthesis.

L9 ANSWER 3 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:192982 BIOSIS
DOCUMENT NUMBER: PREV199698749111
TITLE: Angular furoquinolinones, **psoralen** analogs: Novel antiproliferative agents for skin diseases: Synthesis, biological activity, mechanism of action, and computer-aided studies.
AUTHOR(S): Rodighiero, Paolo; Guiotto, Adriano (1); Chilin, Adriana; Bordin, Franco; Baccichetti, Francarosa; Carllassare,

Francesco; Vedaldi, Daniela; Caffieri, Sergio; Pozzan, A.;
Dall'acqua, Francesco
CORPORATE SOURCE: (1) Dep. Pharmaceutical Sci., Via Fr. Marzolo 5, I-35131
Padova Italy
SOURCE: Journal of Medicinal Chemistry, (1996) Vol. 39, No. 6, pp.
1293-1302.
ISSN: 0022-2623.

DOCUMENT TYPE: Article

LANGUAGE: English

AB With the aim of obtaining new potential photochemotherapeutic agents,
having increased antiproliferative activity and decreased undesired
effects, we have prepared some new furoquinolinones. Two of them have
been

studied in detail: 1,4,6,8-tetramethyl-2H-furo(2,3-h)-quinolin-2-one (8),
and 4,6,8,9-tetramethyl-2H-furo(2,3-h)quinolin-2-one (10). These
compounds

form a molecular complex with DNA, undergoing intercalation inside the
duplex macromolecule, as shown by linear flow dichroism. The complexed
ligands, by subsequent irradiation with UV-A light, photobind with the
macromolecule forming only monocycloadducts with thymine with cis-syn
configuration. In order to evaluate the electronic effects induced by the
nitrogen atom in position 1 of 8, semiempirical calculations have been
performed on both 4,6,4'-**trimethylangelicin** (TMA) and 8. The
results obtained do not clearly differentiate between the two molecules
which, at this level of approximation, show the possibility of
photoreaction with both the 3,4- and 8,9-olefinic bonds for 8 and the

3,4- and 4',5'-bonds for TMA. In the lower energy conformation of intercalated
8, the furan ring is turned toward the minor groove of the
polynucleotide,

in such a way that photoreaction of this ring with thymine is favored.
These compounds unexpectedly inhibit DNA and RNA synthesis in Ehrlich
cells, in the dark. They also show a strong photoantiproliferative
activity, 2 orders of magnitude higher than 8-methoxypsoralen (8-MOP),

the most used drug for photochemotherapy. Their **mutagenic** activity
on Escherichia coli is similar to that of TMA and 8-MOP. On the basis of
these results, the compounds should deserve evaluation of their activity
in the treatment of hyperproliferative skin diseases.

L9 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:837436 CAPLUS

DOCUMENT NUMBER: 123:248523

TITLE: Chemically modified oligonucleotide for site-directed
mutagenesis

INVENTOR(S): Glazer, Peter M.; Havre, Pamela A.

PATENT ASSIGNEE(S): Yale University, USA

SOURCE: PCT Int. Appl., 72 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9501364	A1	19950112	WO 1994-US7234	19940624 <--
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2166079	AA	19950112	CA 1994-2166079	19940624 <--

AU 9473180	A1	19950124	AU 1994-73180	19940624 <--
AU 691194	B2	19980514		
EP 705270	A1	19960410	EP 1994-923258	19940624 <--
EP 705270	B1	19971229		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,

SE

JP 09503644	T2	19970415	JP 1994-503585	19940624 <--
AT 161541	E	19980115	AT 1994-923258	19940624
ES 2113118	T3	19980416	ES 1994-923258	19940624

PRIORITY APPLN. INFO.: US 1993-83088 19930625
WO 1994-US7234 19940624

AB A **mutagenic**, triplex-forming oligonucleotide and methods for it use are provided such that the oligonucleotide is chem. modified to incorporate a **mutagen** and forms a triple-stranded nucleic acid mol. with a specific DNA segment of a target DNA mol. Upon formation of the triplex, the **mutagen** is brought into proximity with the target mol. and causes a mutation at a specific site. The mutation activates, inactivates, or alters the activity and function of the target mol. This process would allow the treatment of genetic disorders by gene therapy without the need for a viral vector. Thus, a **psoralen** (4'-hydroxymethyl-4,5-,8-trimethylpsoralen) was linked via a 2-carbon linker arm to the 5'-phosphate of a 10-mer or 30-mer oligonucleotide targeted to the supF gene (an Escherichia coli amber suppressor tyrosine tRNA gene) for site-specific **mutagenesis** of the lambda phage genome, the pSP189 SV40 vector, or SV40 DNA in monkey

COS cells. After UVA irradiation, sequence analysis of mutations in the target gene showed that almost all were in the targeted region, and 56% were the same T:A to A:T transversion at the targeted base pair with a frequency of 0.233% in lambda phage. Targeted **mutagenesis** occurred even more efficiently in mammalian cells (6% of SV40 genomes) than in bacteria.

L9 ANSWER 5 OF 35 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 95321045 EMBASE

DOCUMENT NUMBER: 1995321045

TITLE: Elimination of potential **mutagenicity** in platelet concentrates that are vitally inactivated with **psoralens** and ultraviolet A light.

AUTHOR: Margolis-Nunno H.; Robinson R.; Ben-Hur E.; Chin S.; Orme T.; Horowitz B.

CORPORATE SOURCE: Lindsley F. Kimball Research Inst., New York Blood Center, 310 East 67th Street, New York, NY 10021, United States

SOURCE: Transfusion, (1995) 35/10 (855-862).
ISSN: 0041-1132 CODEN: TRANAT

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
025 Hematology
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Background: For virus sterilization of platelet concentrates (PCs), treatment with aminomethyltrimethyl **psoralen** (AMT) and long-wavelength ultraviolet A light (UVA) has shown efficacy. It has been found that treatment with 50 pg per mL of AMT and 38 J per cm² of UVA in the presence of 0.35-mM rutin efficiently kills viruses while maintaining platelet integrity. There is, however, concern about the **mutagenic** potential of **psoralens** and UVA (PUVA)-treated PCs. Study Design

and Methods: Adsorption of PUVA-treated PCs with a hydrophobic resin containing C18 as the ligand was used for AMT removal, which was quantitated by the use of radioactive AMT. PUVA-treated PCs, with and without C18 treatment, were examined for solution pH and platelet aggregation response to agonists. In addition, residual AMT activity was determined by AMT's virucidal activity or incorporation into cellular DNA upon a second UVA irradiation and by its **mutagenic** potential in the Ames test. Results: After PUVA treatment of PCs, residual AMT retained

virucidal and adduct-forming ability upon re-exposure to UVA, but activities were less than those observed originally. As has been found previously, AMT had **mutagenic** potential following incubation in the dark with rat liver S9 microsomal enzymes. The PUVA treatment reduced this potential by 90 percent. C18 adsorption following PUVA treatment had no negative effect on platelet integrity and eliminated 50 percent of the added radioactive AMT. In addition, all detectable virucidal, nucleic acid-modifying, and **mutagenic** activities of AMT-treated PCs were removed by C18. Conclusion: These results suggest that hydrophobic resin adsorption of PUVA-treated PCs will conveniently remove functional **psoralens** and eliminates their **mutagenic** potential.

L9 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
ACCESSION NUMBER: 1995:449122 CAPLUS
DOCUMENT NUMBER: 122:259943
TITLE: Genotoxic potential of **psoralen** crosslinks
versus monoadducts in normal human lymphoblasts
AUTHOR(S): Laquerbe, A.; Moustacchi, E.; Papadopoulo, D.
CORPORATE SOURCE: Institut Curie-Biologie, URA 1292 CNRS, 26 rue d'Ulm,
Paris, 75231/05, Fr.
SOURCE: Mutat. Res. (1995), 346(3), 173-9
CODEN: MUREAV; ISSN: 0027-5107
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using the 4,5',8-trimethyl**psoralen** in combination with the reirradn. protocol, we show that, in normal human lymphoblasts, the cytotoxic potential of photoinduced cross-links (CL) is higher than that of monoadducts (MA). In contrast to cytotoxicity, the significant increase in the proportion of CL, at a const. level of total adducts, had no effect on the induction of mutations at the HPRT locus. Comparison with the data obtained in yeast and rodent cells using the same double irradsn. protocol shows that the **mutagenic** potential of CL vs. MA varies between species. This suggests that the equil. between the excision, the recombinational and the **mutagenic** components of the repair pathways which probably det. the **mutagenic** efficiency of CL vs. MA is likely to be species-dependent.

L9 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
ACCESSION NUMBER: 1995:966524 CAPLUS
DOCUMENT NUMBER: 124:78422
TITLE: The **mutagenic** processing of **psoralen**
photolesions leaves a highly specific signature at an
endogenous human locus
AUTHOR(S): Laquerbe, Agnes; Guillouf, Christel; Moustacchi,
Ethel; Papadopoulo, Dora
CORPORATE SOURCE: URA 1292 CNRS, Inst. Curie Section Recherche, Paris,
75231, Fr.
SOURCE: J. Mol. Biol. (1995), 254(1), 38-49
CODEN: JMOBAK; ISSN: 0022-2836
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To assess the role of a given genotoxic agent in the etiol. of human cancers, it is useful to establish the mutational specificity of this agent. The aim of this study was to investigate whether the processing of **psoralen** photolesions, interstrand cross-links (CL) and monoadducts (MA), leaves a specific mol. signature in the mutational events produced at an endogenous locus, HPRT. Human lymphoblasts were treated by 4,5',8-trimethylpsoralen (Me3Pso) in assocn. with a double irradiation protocol (365 plus 365 nm) which allows us to increase the proportion of CL for a given const. no. of total photoadducts. The mol. spectrum of mutations at the HPRT locus induced in these conditions was compared to the previously reported spectra of mutations induced by the same **psoralen** in combination with a single irradiation of either 365 nm (induction of MA and a low proportion of CL) or 405 nm (producing almost exclusively MA). In all treatment conditions, base substitutions constitute the major type of Me3Pso photoinduced mutations. The majority of base substitutions involve a T residue preferably within a 5'-TpA sequence which corresponds to the favored sites of **psoralen** photoadducts. In other words, the Me3Pso photolesions induce at the endogenous HPRT locus a highly specific signature. Moreover, base substitutions have been essentially found in the non-transcribed strand of the HPRT gene suggesting that the **psoralen** photolesions are preferentially removed from the transcribed strand. In spite of the considerable difference between the proportion of lesions of both types (CL or MA) induced in different treatment conditions, the kind of mutations and their sequence distribution are similar suggesting that the mutagenic processing of **psoralen** CL and MA is similar at least for the steps resulting in base substitutions.

L9 ANSWER 8 OF 35 SCISEARCH COPYRIGHT 2001 ISI (R)
 ACCESSION NUMBER: 95:92351 SCISEARCH
 THE GENUINE ARTICLE: QC766
 TITLE: VIRAL INACTIVATION IN PLATELET CONCENTRATES
 AUTHOR: DODD R Y (Reprint)
 CORPORATE SOURCE: AMER RED CROSS, HOLLAND LAB, 15601 CRABBS BRANCH WAY, ROCKVILLE, MD, 20855 (Reprint)
 COUNTRY OF AUTHOR: USA
 SOURCE: TRANSFUSION CLINIQUE ET BIOLOGIQUE, (1994) Vol. 1, No. 3, pp. 181-186.
 ISSN: 1246-7820.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: CLIN
 LANGUAGE: ENGLISH
 REFERENCE COUNT: 23

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although the current risk of posttransfusion infection is very low in North America and Western Europe, there continues to be considerable interest in measures to inactivate residual viruses in blood components. The human immunodeficiency virus is of greatest concern, but hepatitis C virus is also considered to be a significant problem. HTLV-I and -II and HBV may also be transmitted by transfusion, although infrequently. It is likely that effective inactivation methods will have to reduce viral titers by about 5 orders of magnitude, including both viruses found free in plasma and those in intracellular compartments. Although it would be most desirable to have a single procedure to inactivate viruses in all blood components, it appears that different methods may be required for plasma, red cells and platelets. To date, the most promising approach for platelets appears to be photochemical inactivation. In general, photoactive compounds fall into two major groups: photodynamic dyes which

are activated by visible Light and act by oxygen dependent generation of reactive molecular species; and ultraviolet-activated intercalating compounds which form covalent adducts with nucleic acids. We have found that photodynamic inactivators are unable to inactivate viruses in platelet concentrates without damaging the platelets. On the other hand, we have shown that aminomethyl trimethyl psoralen (AMT), when activated by long-wavelength ultraviolet Light (UVA) can inactivate more than 5 logs of model viruses and HIV while platelet in vitro properties are maintained. Further, unlike photodynamic inactivators, AMT is able to inactivate cell-associated and intracellular viruses and also prevents the replication of integrated HIV genome sequences, as demonstrated by PCR. Platelets which have been exposed to antiviral treatment with AMT and UVA also retain their hemostatic effectiveness in an animal model system. One problem with AMT is that it is mutagenic and thus may be inappropriate for infusion into patients. Thus, implementation of a psoralen/UVA inactivation protocol may require the removal of residual drug from the platelet concentrate. An alternate strategy might be to seek psoralens which are non-mutagenic. Finally, in the past year or so, much progress has been made in the use of methylene blue for viral inactivation of plasma. Methylene blue is capable of inactivating free virus in conditions which retain the integrity of platelets.

However,

it appears to be unable to achieve inactivation of intracellular viruses. Consequently, it is unclear when an inactivation method for platelet concentrates could be available for routine use.

L9 ANSWER 9 OF 35 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 3

ACCESSION NUMBER: 94070387 EMBASE

DOCUMENT NUMBER: 1 94070387

TITLE: The study on the effects of psoralen derivatives on epidermal melanocytes in C57 BL mice after topical photochemotherapy.

AUTHOR: Lee S.M.; Hann S.K.; Park Y.K.

CORPORATE SOURCE: Department of Dermatology, Yonsei Univ. College of Medicine, Seoul, Korea, Republic of

SOURCE: Annals of Dermatology, (1994) 6/1 (1-8).

ISSN: 1013-9087 CODEN: ANDEEM

COUNTRY: Korea, Republic of

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 013 Dermatology and Venereology

01 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Background: Monofunctional psoralens plus UVA radiation are not severely phototoxic and have less mutagenic activity than bifunctional psoralens plus UVA radiation. Objective: The purpose of this study was to evaluate pigment producing effect using various concentrations (0.02%, 0.1%, 0.5%) of monofunctional psoralens such as angelicin, khellin and comparing it's effect with TMP in topical photochemotherapy. Method: Ninety-three C57BL mice were painted with either angelicin, khellin or TMP solution in concentrations of 0.02%, 0.1% and 0.5% each and were UVA irradiated. Skin biopsies were performed at 1,3,5 weeks after UVA irradiation. The pigment producing effect were measured by the number, area and perimeter of the melanocytes after topical PUVA. Results: The comparison of melanocyte numbers between different psoralens after five weeks of photochemotherapy showed a significant difference in decreasing order of TMP, khellin and angelicin. The area and perimeter of melanocytes were larger in the TMP group after five weeks photochemotherapy than the other

group. However in the khellin and angelicin group, the area and perimeter of melanocytes were not increased by increasing the frequency of the UVA irradiation. Conclusion: The number, area and perimeter of melanocytes after topical PUVA increased in the TMP group compared to angelicin or khellin group. We expect the clinical application of angelicin and khellin in vitiligo is possible considering the result of the study of pigment producing effect with a higher concentration and higher dose of UVA.

L9 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:46852 CAPLUS

DOCUMENT NUMBER: 120:46852

TITLE: Targeted **mutagenesis** of simian virus 40 DNA mediated by a triple helix-forming oligonucleotide

AUTHOR(S): Havre, Pamela A.; Glazer, Peter M.

CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06510, USA

SOURCE: J. Virol. (1993), 67(12), 7324-31

CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Triple-helical DNA can be formed by oligonucleotides that bind as third strands of DNA in a sequence-specific manner in the major groove in homopurine/homopyrimidine stretches in duplex DNA. Such triple helix-forming oligonucleotides have been used to inhibit gene expression by blocking transcription factor access to promoter sites in transient expression assays. In an alternative approach to genetic manipulation using triplex DNA, the triplex-forming oligonucleotides were used to produce site-specific, targeted mutations in a viral genome in order to achieve a permanent, heritable effect on gene function and expression. A triplex-forming oligonucleotide linked to a **psoralen** deriv. at its 5' end was used to achieve targeted **mutagenesis** in a simian virus 40 (SV40) vector genome. Site-specific triplex formation delivers the **psoralen** to the targeted site in the SV40 DNA. Photoactivation of the **psoralen** yields adducts and thereby mutations at that site. Mutations were produced in the target gene in

>6%

of the viral genomes. DNA sequence anal. of the mutations in the target gene showed that all were in the targeted region, and 55% the same T:A-to-A:T transversion precisely at the targeted base pair. In control expts., no **mutagenesis** above the background frequency in the assay was produced by a non-triplex-forming, **psoralen**-linked oligonucleotide. Unless a vast excess of this oligonucleotide was used, demonstrating the specificity of the targeted **mutagenesis**. This frequency of targeted **mutagenesis** of SV40 in monkey cells represents a 30-fold increase relative to similar expts. using λ phage in bacteria, suggesting that fixation of the triplex-directed

lesion

into a mutation occurs more efficiently in mammalian cells. If the ability to reproducibly and predictably target mutations to sites in

viral

DNA in vitro by using modified oligonucleotides can be extended to DNA in vivo, this approach may prove useful as a technique for gene therapy, as

a

strategy for antiviral therapeutics, and as a tool for genetic engineering.

L9 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2001 ACS

DUPLICATE 4

ACCESSION NUMBER: 1993:490188 CAPLUS

DOCUMENT NUMBER: 119:90188

TITLE: Determination of residual 4'-aminomethyl-4,5',8-

trimethylpsoralen and mutagenicity
 testing following psoralen plus UVA
 treatment of platelet suspensions
 AUTHOR(S): Wagner, Stephen J.; White, Randy; Wolf, Ludwig;
 Chapman, John; Robinette, Daniel; Lawlor, Timothy E.;
 Dodd, Roger Y.
 CORPORATE SOURCE: Jerome H. Holland Lab., Am. Red Cross Blood Serv.,
 Rockville, MD, 29855, USA
 SOURCE: Photochem. Photobiol. (1993), 57(5), 819-24
 CODEN: PHCBAP; ISSN: 0031-8655
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB **Psoralens** and UVA light have been used in the lab. to study the
 inactivation of viruses that may be infrequently present in platelet
 concs. that are prepd. for transfusion. To evaluate safety aspects of
 the treatment of platelet suspensions with 4'-aminomethyl-4,5',8-
trimethylpsoralen (AMT), residual levels and **mutagenic**
 potential of AMT are examd. after UVA phototreatment.
 4'-Aminomethyl-4,5',8-**trimethylpsoralen**, at a final concn. of 40
 .mu.g/mL, was added to platelet suspensions which contained 16% plasma
 and a synthetic medium. Platelet suspensions contg. AMT were irradiated with
 up to 7.2 J/cm² UVA light under normal oxygen levels. Residual levels of
 AMT were detd. by HPLC and a bioassay based on bacteriophage .phi.6
 inactivation. The photodestruction of AMT or its activity by UVA was
 characterized by a D37 value of 0.6 and 0.3 J/cm² with HPLC or bioassay,
 resp. At 2.4 J/cm² UVA, which results in .apprx.5 log₁₀ inactivation of
 vesicular stomatitis virus (VSV) and retention of platelet in vitro
 properties, 12% (HPLC) to 9% (bioassay) AMT remained. Like other
psoralens, AMT was found to bind to serum proteins as shown by
 ultrafiltration. Results are consistent with .apprx.36% of the initial
 drug load binding primarily to serum albumin. It was detd. using 3H-AMT
 that 9-18% of radioactivity was bound to platelets in the absence of
 irradiation. Similar fractions (13-18%) of AMT were bound to platelets after
 3.6 J/cm² UVA irradiation, and 8-10% of total AMT was assocd. with
 saline-washed irradiated platelets and is presumably tightly bound.
Mutagenicity testing (Ames test, in the absence of UVA) was also
 carried out on the UVA irradiated platelet samples. With Salmonella
 tester strains which detect primarily base substitution mutations (TA100,
 TA1535 and TA102), no increase from background **mutagenesis**
 levels was obsd. with any of the samples. However, tester strains which
 detect frameshift mutations (TA98, TA1537, and TA1538) displayed
 significant increases in histidine revertants over background levels for
 irradiated and nonirradiated AMT-contg. samples tested in the presence of
 S9 microsomal enzymes. In the absence of S9 activation, a
mutagenic response was obsd. only with tester strain TA1537. All
 frameshift tester strains exhibited decreased nos. of induced revertants
 with lower residual AMT concns. (which correlated with higher UVA dose).
 Significant **mutagenesis** was still obsd. for platelet suspensions
 irradiated with virucidal levels of UVA which maintain platelet in vitro
 function (2.4 J/cm²). These results suggest that residual available AMT
 is **mutagenic** in the Ames test and that the obsd. frameshift
 mutations may be caused by binding of AMT or its metabolites to nucleic
 acids in the absence of UVA light.

L9 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 5
 ACCESSION NUMBER: 1994:128597 CAPLUS
 DOCUMENT NUMBER: 120:128597
 TITLE: Mutagenic processing of psoralen

AUTHOR(S): monoadducts differ in normal and Fanconi anemia cells
Guillouf, Christel; Laquerbe, Agnes; Moustacchi,
Ethel; Papadopoulos, Dora
CORPORATE SOURCE: Sect. Biol., Inst. Curie, Paris, 75231, Fr.
SOURCE: Mutagenesis (1993), 8(4), 355-61
CODEN: MUTAEX; ISSN: 0267-8357
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mol. spectra of mutations photoinduced (405 nm) by 4,5',8-
trimethylpsoralen monoadducts (MA), at an endogenous locus,
hypoxanthine-guanine phosphoribosyltransferase (HPRT) in normal and in a
Fanconi anemia (FA) lymphoblast cell line, complementation group D, are
presented. The authors show that, in normal cells, MA induce only base
substitutions. In contrast, in FA cells which are partially deficient in
the incision of MA, deletions are preferentially induced over point
mutations (62% of the total). Although the proportion of base
substitutions is lower in FA cells, their type and sequence distribution
are similar in FA and normal cell lines. The majority of base
substitutions are located at sites of **psoralen** MA which suggest
that 4,5',8-**trimethylpsoralen** photoinduced mutations are
targeted and preferentially formed in the nontranscribed strand.
Moreover, point mutations induced by MA in normal and FA cells are not
homogeneously distributed, they preferentially occur in exon 8 of the
HPRT gene. This heterogeneous distribution of mutations is ascribed to
processing of MA. Great similarities were found between normal and FA
cells with respect to the nature and location of point mutation at the
HPRT gene; the high proneness to deletions remains one of the major
instability features of FA.

L9 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 6

ACCESSION NUMBER: 1993:532862 CAPLUS

DOCUMENT NUMBER: 119:132862

TITLE: Molecular spectrum of mutations induced at the HPRT
locus by a cross-linking agent in human cell lines
with different repair capacities

AUTHOR(S): Papadopoulos, D.; Laquerbe, A.; Guillouf, C.;
Moustacchi, E.

CORPORATE SOURCE: Inst. Curie - Biol., CNRS, Paris, Fr.

SOURCE: Mutat. Res. (1993), 294(2), 167-77

CODEN: MUREAV; ISSN: 0027-5107

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mol. characterization of mutations photoinduced by a crosslinking agent,
4,5',8-**trimethylpsoralen** (Me3Pso), in normal human lymphoblasts
was conducted in parallel with lymphoblasts derived from Fanconi anemia
patients. Such cells have been previously described to be impaired in
repair of **psoralen** photolesions. The endogenous HPRT locus was
used as a target gene. The treatment of cells with Me3Pso in combination
with 365 nm irradiation leads to the formation of interstrand cross-links,

and

specific monoadducts. The authors anal. revealed that the
mutagenic processing of Me3Pso photoadducts in normal human cells
results essentially in base substitutions (84%). These are localized to
sequences shown previously to be favored for the formation of Me3Pso
monoadducts. The **mutagenic** processing of the same lesions in
Fanconi anemia cells results in fewer base substitutions (22%), with
deletions (66%) being the predominant class of mutation. In contrast to
prokaryotic systems, frameshifts are poorly represented among Me3Pso
induced mutations in human cells. In spite of important differences

between the kinds of mutations obsd. in the two cell lines, the authors anal. reveals similarities in the type of base substitutions and their sequence distribution. In both normal and Fanconi anemia cell lines mutations, mostly targeted on thymine residues, are preferentially located on the non-transcribed strand.

L9 ANSWER 14 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:432642 BIOSIS
DOCUMENT NUMBER: PREV199396087267
TITLE: Cytogenetic evidence for differences in DNA incision activity in xeroderma pigmentosum group A, C and D cells after X-irradiation during G-2 phase.
AUTHOR(S): Parshad, R. (1); Tarone, R. E.; Price, F. M.; Sanford, K. K.
CORPORATE SOURCE: (1) Lab. Cell. Mol. Biol., Natl. Cancer Inst., Bethesda, MD
20892 USA
SOURCE: Mutation Research, (1993) Vol. 294, No. 2, pp. 149-155.
ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The capacity of cells to incise DNA to remove altered sites after DNA damage can be determined from the rate of DNA-strand break accumulation in the presence of an inhibitor of DNA-repair synthesis, such as 1-beta-D-arabino-furanosylcytosine (ara-C). Because each chromatid contains a single continuous molecule of double-stranded DNA, chromatid breaks and gaps, i.e., non-displaced breaks, represent unrepaired DNA-strand breaks. The accumulation of chromatid breaks and gaps after X-irradiation in the presence of ara-C thus provides a measure of DNA incision activity. Addition of ara-C to skin fibroblasts or stimulated blood lymphocytes from normal individuals at intervals after X-irradiation significantly increased frequencies of chromatid breaks and/or gaps. In contrast, addition of ara-C to XP cells of complementation groups A and D had a negligible effect and a significant but less than normal effect on XP cells of complementation group C and one sample of blood lymphocytes of undetermined complementation group. The results thus show negligible incision activity after G-2 phase X-irradiation in XP-A and XP-D cells and a level higher but less than normal in XP-C cells.

L9 ANSWER 15 OF 35 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1993:286820 BIOSIS
DOCUMENT NUMBER: PREV199345004945
TITLE: Mutagenic processing of **psoralen** monoadducts differ in normal and Fanconi anemia cells.
AUTHOR(S): Guilouf, C.; Papadopoulo, D.; Laquerbe, A.; Moustacchi, E.
CORPORATE SOURCE: Inst. Curie Biol., Paris France
SOURCE: Environmental and Molecular Mutagenesis, (1993) Vol. 21, No. SUPPL. 22, pp. 26.
Meeting Info.: 24th Annual Scientific Meeting of the Environmental Mutagen Society Norfolk, Virginia, USA April 7-22, 1993
ISSN: 0893-6692.
DOCUMENT TYPE: Conference
LANGUAGE: English

L9 ANSWER 16 OF 35 MEDLINE DUPLICATE 7
 ACCESSION NUMBER: 93191862 MEDLINE
 DOCUMENT NUMBER: 93191862 PubMed ID: 1294168
 TITLE: Photobiological activity of certain new
 methylazapsoralens.
 AUTHOR: Laccichetti F; Bordin F; Simonato M; Toniolo L; Marzano C;
 Lodighiero P; Chilin A; Carlassare F
 CORPORATE SOURCE: Department of Pharmaceutical Sciences, Padua University,
 Italy.
 SOURCE: FARMACO, (1992 Dec) 47 (12) 1529-41.
 Journal code: ACZ; 8912641. ISSN: 0014-827X.
 PUB. COUNTRY: Italy
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 9904
 ENTRY DATE: Entered STN: 19930423
 Last Updated on STN: 19930423
 Entered Medline: 19930413

AB The photobiological activity of a series of **psoralen** isomers
 carrying a nitrogen atom at 8 position, new potential drugs for the
 photochemotherapy of hyperproliferative skin diseases, have been studied;
 the more active derivatives appeared to be 5,4'-dimethyl-8-azapsoralen
 and 3,4,4'-**trimethyl-8-azapsoralen** which induced a strong inhibition
 of DNA synthesis in Ehrlich ascites cells, very similar to that provoked
 by 8-methoxypsoralen, the furocoumarin at present used in
 photochemotherapy. Such compounds induced a small amount of inter-strand
 DNA cross-links and were non phototoxic when assayed on guinea-pig skin;
 however, both derivatives appeared to be highly **mutagenic** in E.
 coli WP2 TM6. This strain contains the plasmid R46 and it is proficient
 in DNA repair, and therefore monoadducts do not should be **mutagenic**
 in such a strain. Because the first steps of excision, which remove
 monoadducts, and of the main cross-link repair use the same enzymes
 (produced by the uvrABC complex), in the presence of a great number of
 monofunctional lesions, it is possible that there are not sufficient
 enzyme molecules for removing cross-links according this pathway, which
 could be repaired by a second one, uvrABC independent and based on
 glycosylase activity, which works at reduced levels and is much less
 accurate.

L9 ANSWER 17 OF 35 PLEASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 ACCESSION NUMBER: 2000183 EMBASE
 DOCUMENT NUMBER: 990435183
 TITLE: Molecular analysis of mutations induced by
 8-hydroxymethyl-4,5',8-**trimethylpsoralen** and UVA
 in the mouse HPRT gene.
 AUTHOR: Lete J.
 CORPORATE SOURCE: Laboratory of Microbiology, Institute of Pathology,
 University of Liege, B-4000 Liege, Belgium
 SOURCE: Journal of Photochemistry and Photobiology B: Biology,
 1999, 12/1 (37-55).
 ISSN: 1011-1344 CODEN: JPPBEG
 COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 3 Dermatology and Venereology
 2 Human Genetics
 1 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The effects of the reaction photosensitized by 4'-hydroxymethyl-4,5',8-trimethylpsoralen (HMT) on a mouse lymphoma cell line have been examined. Using the hypoxanthine phosphoribosyltransferase (HPRT) locus as

target gene, a mutagenic effect of the photoreaction can be detected concomitantly with a loss of cell viability. Isolation of HPRT deficient clones has permitted a molecular characterization of the mutational pattern induced by the photosensitization reaction mediated by HMT. Southern blotting analysis demonstrated that the HPRT deficiency could not be correlated with gene deletions larger than 300 bp. Using polymerase chain reaction on both DNA and cDNA, amplification products have been cloned into M13mp18 and sequenced. Base transversions targeted on thymine residues have been located in exon 2, 3, 8 and 9 together with spontaneous frameshift mutations occurring in a run of guanine residues

in exon 3. HPRT deficiencies owing to mutations arising in the HPRT promoter region have also been observed. Dot and Northern blot analysis revealed that the photoreaction could lead to either a reduced level of gene transcription or a complete absence of HPRT m-RNA. Using polymerase chain reaction for amplification and agarose gel electrophoresis, deletions in the HPRT promoter have been observed and correlated to deficient enzyme expression.

L9 ANSWER 18 OF 35

MEDLINE

DUPLICATE 8

ACCESSION NUMBER: 89789 MEDLINE

DOCUMENT NUMBER: 789 PubMed ID: 1821628

TITLE: Psoralens: new potential photochemotherapeutic agents for psoriasis.

AUTHOR: Giordano D; Caffieri S; Miolo G; Dall'Acqua F; Baccichetti F; Diotto A; Benetollo F; Bombieri G; Recchia G; Ricciofolini M

CORPORATE SOURCE: Department of Pharmaceutical Sciences of the University, Padova, Italy.

SOURCE: J CO, (1991 Dec) 46 (12) 1407-33.

ISSN: 0014-827X; ISSN code: ACZ; 8912641. ISSN: 0014-827X.

PUB. COUNTRY: Italy

ARTICLE TYPE: Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Psoriasis Journals

ENTRY MONTH: 1991

ENTRY DATE: 1991 STN: 19920911

Updated on STN: 19920911

Updated Medline: 19920824

AB New bioisoters of psoralen, obtained by replacing carbon 8 of the central benzene ring with a nitrogen, were studied from the photochemical, biological and phototherapeutic points of view. In particular, 4,4',5'-dimethyl, 4,4',5'-trimethyl and 3,4,4',5'-tetramethylazapsoralen were studied. The crystal and molecular structure of 4,4',5'-trimethylazapsoralen, obtained by X ray diffraction, was reported. Like psoralen, these compounds form a molecular complex with DNA, undergoing intercalation inside the double helix of the macromolecule. When irradiated with long ultraviolet light (365 nm), the intercalated drug photoconjugates covalently to the macromolecule, forming mono- and diadducts. The photobinding rate show

the following order of magnitude: 4,4',5'-trimethylazapsoralen (4,4',5'-TMAP)

=

3,4,4',5'-tetramethylazapsoralen (3,4,4',5'-TMAP) greater than 4',5'-dimethylazapsoralen (4',5'-DMAP) = 4,4'-dimethylazapsoralen (4,4'-DMAP). The DNA photobinding rate of 8-methoxypsoralen (8-MOP), taken as reference compound, is similar to that of the two dimethylazapsoralens but lower than that of the dimethyl and tetramethyl derivatives. The ability of azapsoralens to induce cross-links in DNA is lower than that of 8-MOP. However, capacity to induce cross-links does not parallel the DNA photobinding rate; it is higher for trimethyl derivative and lower for tetramethyl derivative. Azapsoralens show evident antiproliferative activity. The trimethyl derivative is the most active, followed by tetramethyl, with these compounds showing activity slightly higher than that of 8-MOP. The two dimethyl derivatives are less active. The mutagenic activity of azapsoralens on E. coli WP2 TM6 is lower than that of 8-MOP in the same conditions. The new compounds do not show any skin phototoxicity on guinea pig skin. On the basis of its DNA photobinding, antiproliferative activity, mutagenicity and lack of skin phototoxicity, 3,4,4',5'-TMAP was chosen for clinical evaluation. Clinical results obtained by topical treatment of psoriatic plaques reveal evident therapeutic effectiveness and clearing is between good and moderate, although 8-MOP, used as reference compound, is more effective.

L9 ANSWER 19 OF 39 MEDLINE
 ACCESSION NUMBER: 247241 MEDLINE
 DOCUMENT NUMBER: 247241 PubMed ID: 1811623
 TITLE: Angelicins: structure activity studies on the role of methyl groups present in 3,4 and 4',5' photoreactive sites.
 AUTHOR: Baldi D; Dall'Acqua F; Baccichetti F; Carllassare F; Cusi F; Rodighiero P; Manzini P; Guiotto A
 CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Rome, Italy.
 SOURCE: J Pharm Med, (1991 Nov) 46 (11) 1381-406.
 PUB. COUNTRY: Italy
 PUB. NUMBER: 0014-827X.
 LANGUAGE: English; Article; (JOURNAL ARTICLE)
 FILE SEGMENT: Full Text
 ENTRY MONTH: Nov
 ENTRY DATE: 1991
 STN: 19920619
 Updated on STN: 19920619
 Medline: 19920609

AB The effect of the introduction of one, two or three methyl groups at the level of 3,4 or 4',5' photoreactive site of angelicin, in terms of extent of intercalation and DNA-photobinding, was studied. The introduction of one methyl group both in the 3 or 4 and in 4' or 5' position increases the affinity of angelicin toward DNA for the molecular complex formation and enhances the DNA photobinding, even if to a different extent. The increase is more pronounced for occupancy of 5' or 4' position; much less pronounced is the enhancement in the case of 3 or 4 positions. The introduction of two methyl groups in 3,4 or in 4',5' positions leads to an increased capacity to form the intercalated complex with DNA; the photoreactivity is also enhanced, but to a larger extent for 4',5'-dimethylangelicin. No steric hindrance, therefore, seems to be

exerted by the introduction of one or two methyl groups at the level of the photoreactive moieties of angelicin. The introduction of a third methyl group in 4',5'-trimethyl or in 3,4-dimethylangelicin exhibits a strong enhancement of DNA photobinding; in particular 4,4',5'-**trimethylangelicin** appears the most photoreactive towards DNA. Angelicins carrying methyl groups in 3,4 positions exhibit lower antiproliferative activity than derivatives carrying methyl groups in 4',5' positions. No correlation was observed between antiproliferative activity and DNA photobinding; may be that the presence of methyl groups in 3,4 or in 4',5' positions affects the type of cycloadducts formed. The different ratios of adducts may affect the antiproliferative effect. (ABSTRACT TRUNCATED AT 250 WORDS)

L9 ANSWER 20 OF 30 MEDLINE
 ACCESSION NUMBER: 122790 MEDLINE
 DOCUMENT NUMBER: 122790 PubMed ID: 2027904
 TITLE: 4,4',5'-**trimethyl**-8-azapsoralen, a more photoreactive and non-skin-phototoxic bifunctional isomer of **psoralen**.
 AUTHOR: Dall'Acqua F; Caffieri S; Baccichetti F; Bordin F; Chilini A; Guiotto A
 CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Bologna, Italy.
 SOURCE: JOURNAL OF CHEMISTRY AND PHOTOBIOLOGY, (1991 Jan) 53 (1) 3-8.
 PUB. COUNTRY: United Kingdom
 LANGUAGE: English
 FILE SEGMENT: Journal Articles
 ENTRY MONTH: January
 ENTRY DATE: 1991
 STN: 19910630
 MEDLINE: 19910610

AB Photochemical and photobiological properties of a new isomer of **psoralen**, 4,4',5'-**trimethyl**-8-azapsoralen (4,4',5'-TMAP), have been studied. This compound shows a high DNA-photobinding ability, higher than that of 8-methoxypsoralen (8-MOP), forming both intra-strand and inter-strand cross-links. The yield of cross-links, however, is markedly lower than that of 8-MOP. Antiproliferative activity of 4,4',5'-TMAP, in terms of DNA synthesis inhibition in human ascites tumor cells, is higher than that of 8-MOP. **Mutagenic** activity of E. coli WP2 R46+ cells appeared similar to or even lower than that of 8-MOP. This new compound applied on depilated guinea pig skin and irradiated with UVA did not show any skin-phototoxicity. On the basis of these properties 4,4',5'-TMAP appears to be a potential photochemotherapeutic agent.

L9 ANSWER 21 OF 30 RESEARCH COPYRIGHT 2001 ISI (R)
 ACCESSION NUMBER: 725 SCISEARCH
 THE GENUINE ARTICLE: 725
 TITLE: MIC IMMUNOSUPPRESSION OF CELL-MEDIATED HYPERSENSITIVITY REACTIONS BY A MONOFUNCTIONAL **PSORALEN** DERIVATIVE ULTRAVIOLET-A RADIATION
 AUTHOR: KIMURA S E (Reprint)
 CORPORATE SOURCE: TEXAS, MD ANDERSON CANC CTR, DEPT IMMUNOL, BOX 178, 1600 HOLCOMBE BLVD, HOUSTON, TX, 77030 (Reprint)
 COUNTRY OF AUTHOR: USA
 SOURCE: JOURNAL OF DERMATOLOGY PHOTOIMMUNOLOGY & PHOTOMEDICINE, (1991) Vol. 8, No. 3, pp. 116-122.

0108-9684.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT:
LANGUAGE: English
REFERENCE COUNT: 17

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Because of the undesirable side effects associated with the use of 8-methoxypsoralen and long-wave ultraviolet A (UVA) radiation in the treatment of skin disorders such as psoriasis, the use of monofunctional **psoralens**, which are less erythemogenic, less **mutagenic**, and generally less phototoxic, has received considerable attention. Little is known, however, about the immunosuppressive properties of monofunctional **psoralens**. The purpose of this study was to examine the effect of parenteral administration of a monofunctional **psoralen**, angelicin, plus exposure to UVA radiation on the immune response. Injection of angelicin followed by exposure to UVA radiation significantly depressed delayed-type hypersensitivity to alloantigen in a dose-dependent fashion. Similarly, the capacity of spleen cells from the angelicin and UVA-treated **animals** to proliferate to alloantigen was significantly depressed. The suppression was specific for the alloantigen used to sensitize the angelicin and UVA-treated **animals** and was associated with the appearance of splenic antigen-specific suppressor T lymphocytes. These data demonstrate that the effect of systemic administration of a monofunctional **psoralen** followed by UVA exposure on the immune response is similar to that seen following the administration of bifunctional **psoralens**. These findings also suggest that the severe skin phototoxicity associated with the use of a bifunctional **psoralen** and UVA radiation is not necessary for the induction of systemic immunosuppression. Furthermore, the induction of systemic antigen-specific immunosuppression by angelicin plus UVA, without the skin phototoxicity, suggests the possibility of using this and related compounds to specifically inhibit unwanted immune reactions.

L9 ANSWER 22 OF 1 MEDLINE
ACCESSION NUMBER: 1990 71 MEDLINE
DOCUMENT NUMBER: 1990 71 PubMed ID: 2337519
TITLE: 6-Methylangelicins: new monofunctional
or chemotherapeutic agents for psoriasis.
COMMENT: Reported in: Br J Dermatol. 1991 Jan;124(1):112-3
AUTHOR: Folini M; Recchia G; Boi S; Pisciolli F; Bordin F;
Cocchetti F; Carllassare F; Tamaro M; Pani B; Baburdi N;
+
CORPORATE SOURCE: Division of Dermatology, Hospital of Santa Chiara, Trento,
Italy.
SOURCE: BRITISH JOURNAL OF DERMATOLOGY, (1990 Apr) 122
112-3-24.
Accession code: AW0; 0004041. ISSN: 0007-0963.
PUB. COUNTRY: United Kingdom
Article; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Society Journals
ENTRY MONTH: April
ENTRY DATE: 1990 STN: 19900720
Updated on STN: 19900720
Medline: 19900615
AB The monofunctional coumarins, the 6-methylangelicins, were tested for their antiproliferative activity with various **animal** models and

for genotoxicity in micro-organisms and in mammalian cells. The most active compounds were 4,4'-**trimethylangelicin**, which showed a high antiproliferative effect and reduced genotoxicity in comparison with 8-methoxypsoralen (8-MOP). Some of these compounds were also tested clinically by topical application on 17 patients with psoriasis. They appeared to be more effective than 8-MOP in clearing psoriasis without inducing skin toxicity. The methylangelicins also caused skin pigmentation.

L9 ANSWER 23 OF 3 MEDLINE
 ACCESSION NUMBER: 199003 MEDLINE
 DOCUMENT NUMBER: 199003 PubMed ID: 2121936
 TITLE: Effect of furocoumarin-plus-UVA-induced damage and mutagenic consequences in eukaryotic cells.
 AUTHOR: Wenzel D; Dardalhon M; Magana-Schwencke N
 CORPORATE SOURCE: Institut Curie-Section de Biologie, CNRS UA 1292, Paris, France.
 SOURCE: JOURNAL OF PHOTOCHEMISTRY AND PHOTOBIOLOGY. B, BIOLOGY, (1990 Jun) 6 (1-2) 221-36.
 Journal code: JLI; 8804966. ISSN: 1011-1344.
 PUB. COUNTRY: France
 PUB. TYPE: Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Society Journals
 ENTRY MONTH: June
 ENTRY DATE: Indexed STN: 19910208
 Last updated on STN: 19910208
 Entered Medline: 19901213

AB In the presence of near-UV radiation (UVA) furocoumarins (**psoralens**) produce the defined lesions in DNA, i.e. monoadducts and interstrand crosslinks. Their use in photochemotherapy (**psoralen** plus UVA treatment) and cosmetics raises questions concerning the reversibility of these lesions and their genotoxic consequences. We have analysed the repair of **psoralen** photoadducts in cultured eukaryotic cells, such as yeast and mammalian cells, for furocoumarins of photochemotherapeutic interest. In yeast, the interaction of repair pathways differs in exogenous (plasmid) and endogenous (chromosomal) DNA. The order of **mutagenic** activity is 4,5',8-trimethylpsoralen greater than 5-methoxypsoralen greater than 8-methoxypsoralen greater than 7-methylpyrido[3,4-c]psoralen greater than 8-methoxypsoralen. The **mutagenicity** is dependent on **psoralen** reversibility, concentration and bioavailability, maximal UVA dose, wavelength, dose (fluence) rate and presence or absence of chemical inducers. It probably involves an inducible component. Chromosome breakage occurs during the repair period after PUVA treatment. It appears that the genotoxic effects of **psoralens** are produced by a specific treatment of induced photolesions and the interaction of different repair systems.

L9 ANSWER 24 OF 3 MEDLINE DUPLICATE 9
 ACCESSION NUMBER: 1995 MEDLINE
 DOCUMENT NUMBER: 1995 PubMed ID: 2125562
 TITLE: Biological studies with dioxetanes in isolated DNA, bacteria, and mammalian cells.
 AUTHOR: Muller E; Beinbauer A; Mosandl T; Saha-Moller C; Vargas F; Muller E; Schiffmann D; Wild D
 CORPORATE SOURCE: Institute of Organic Chemistry, University of Wurzburg, 97082 Wurzburg, Federal Republic of Germany.
 SOURCE: ENVIRONMENTAL HEALTH PERSPECTIVES, (1990 Aug) 88
 Ref: 32

PUB. COUNTRY: United States
Journal code: EIO; 0330411. ISSN: 0091-6765.

Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
REVIEW, TUTORIAL)

LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199101

ENTRY DATE: Entered STN: 19910329

Last updated on STN: 19910329

Entered Medline: 19910228

AB 1,2-Dioxetanes are efficient chemical sources of triplet excited carbonyl compounds, which are observed to be genotoxic in isolated DNA, bacteria, and cultured mammalian cells. In superhelical DNA of bacteriophage PM2, various alkyl- and hydroxyalkyl-substituted dioxetanes (1) induced predominantly endonuclease-sensitive base modifications and only few single strand breaks. With a specific endonuclease a small fraction of the base modifications was identified as pyrimidine dimers. The **psoralen** dioxetane (2a) or PsD bound photochemically to calf thymus DNA at the alpha-pyrone ring of **psoralen** (fluorescence measurements). Photobinding was also observed when calf thymus DNA was incubated with **psoralen** and 3-hydroxymethyl-3,4,4-trimethyl-1,2-dioxetane. In Syrian hamster embryo fibroblasts and HL-60 cells, dioxetanes induced DNA single strand breaks. The alkyl- and hydroxyalkyl-substituted dioxetanes 1 and 2 were efficiently inactivated by cysteine, glutathione, ascorbic acid, tocopherol, NADH and FADH2.

While dioxetanes 1 and 2 were not **mutagenic** in Salmonella typhimurium strain TA100, benzofuran dioxetanes 3 exhibited substantial effects. Further data imply that presumably a **mutagenic** intermediate with a lifetime of a few minutes is produced from the benzofuran dioxetane.

L9 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:169398 CAPLUS

DOCUMENT NUMBER: 10:169398

TITLE: Multiplicity reactivation and **mutagenesis** of trimethyl**psoralen**-damaged herpes virus in normal and Fanconi's anemia cells

AUTHOR(S): Poppey, J.; Sala-Trepat, M.; Lopez, B.

CORPORATE SOURCE: Inst. Curie, Paris, 75231, Fr.

SOURCE: **Mutagenesis** (1989), 4(1), 67-71

CODEN: MUTAEX; ISSN: 0267-8357

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fanconi's anemia (FA) cells are hypersensitive to the lethal effect of DNA

crosslinking compds. Herpes simplex virus (HSV) has been used here as a probe to monitor repair of **psoralen** damage in FA cells, including **psoralen** crosslinks. The replication of HSV is impaired when its DNA contains covalently photobound **psoralen** mols. In comparison to other **psoralens**, 4,5',8-trimethyl**psoralen** (TMP) is 1 of the most photoreactive **psoralens** and it forms a relatively high proportion of DNA interstrand crosslinks with UVA irradiation (365 nm). TMP-damaged HSV is efficiently reactivated by multiple infection in human fibroblasts. The extent of multiplicity reactivation is greater in cells from FA donors (5 strains tested) than in normal cells (3 strains). **Mutagenesis** studied in the viral thymidine kinase focus revealed the following: (1) the spontaneous viral mutation rate is lower in FA than in normal cells;

and (2) under conditions of multiple infection, the mutation rate is either greater (normal cells) or unchanged (FA cells) in the progeny from **psoralen**-damaged HSV compared to that from untreated virus. taken together, these observations suggest that the pathway underlying multiplicity reactivation of **psoralen**-damaged HSV is error-free in FA cells relative to normal cells.

L9 ANSWER 26 OF 5 CAPLUS COPYRIGHT 2001 ACS
 ACCESSION NUMBER: 1988:50501 CAPLUS
 DOCUMENT NUMBER: 198:50501
 TITLE: Processing of **psoralen** adducts in an active human gene: repair and replication of DNA containing monoadducts and interstrand cross-links
 AUTHOR(S): Mos, Jean Michel H.; Hanawalt, Philip C.
 CORPORATE SOURCE: Dep. Biol. Sci., Stanford Univ., Stanford, CA, 94305, USA
 SOURCE: Cell (Cambridge, Mass.) (1987), 50(5), 799-99
 CODEN: CELLB5; ISSN: 0092-8674
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB DNA repair was examined in the dihydrofolate reductase (DHFR) gene in cultured human cells treated with 4'-hydroxymethyl-4,5',8-**trimethylpsoralen** (HMT) using a newly developed assay for interstrand DNA cross-linking in defined genomic sequences. Within 24 h, 80% of the cross-links, but only 45% of the monoadducts, were removed from a 32 kb transcribed sequence, demonstrating that repair efficiency in an active human gene varies with the nature of the damage. HMT monoadducts were also detected in the replicated DHFR sequence at frequencies indicating little interference with replication. The existence of cross-linked monoadduct sites in the replicated DNA implies strand continuity opposite those sites and a relatively error-free mechanism of bypass. Thus lesion replication could circumvent transcription blockage in a damaged gene. These findings have important implications for mechanisms of **mutagenesis** and DNA lesion tolerance in human cells.

L9 ANSWER 27 OF 5 MEDLINE
 ACCESSION NUMBER: 8722049 MEDLINE
 DOCUMENT NUMBER: 8722049 PubMed ID: 3473014
 TITLE: 4,5',8-**Trimethylpsoralen**.
 AUTHOR: Anonymous
 SOURCE: IARC MONOGRAPHS ON THE EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO HUMANS, (1986) 40 357-71.
 Journal code: GE4; 7902489. ISSN: 0250-9555.
 PUB. COUNTRY: Switzerland
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198707
 ENTRY DATE: Entered STN: 19900305
 Last Updated on STN: 19900305
 Entered Medline: 19870716

L9 ANSWER 28 OF 5 MEDLINE
 ACCESSION NUMBER: 8722045 MEDLINE
 DOCUMENT NUMBER: 8722045 PubMed ID: 3473010
 TITLE: Angelicin and some synthetic derivatives.
 AUTHOR: Anonymous

SOURCE: IARC MONOGRAPHS ON THE EVALUATION OF THE CARCINOGENIC RISK
OF CHEMICALS TO HUMANS, (1986) 40 291-315.
Journal code: GE4; 7902489. ISSN: 0250-9555.

PUB. COUNTRY: Switzerland
Journal ; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198707

ENTRY DATE: Entered STN: 19900305
Last updated on STN: 19900305
Entered Medline: 19870716

L9 ANSWER 29 OF 35 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 85173673 EMBASE

DOCUMENT NUMBER: 1985173673

TITLE: **Psoralens** as photoactive probes of nucleic acid
structure and function: Organic chemistry, photochemistry,
and biochemistry.

AUTHOR: Cimino G.D.; Gamper H.B.; Isaacs S.T.; Hearst J.E.

CORPORATE SOURCE: Department of Chemistry, University of California,
Berkeley, CA 94720, United States

SOURCE: Annual Review of Biochemistry, (1985) VOL. 54/-
(1151-1193).

CODEN: ARBOAW

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index

029 Clinical Biochemistry

LANGUAGE: English

AB **Psoralens** comprise the most important class of photochemical reagents for the investigation of nucleic acid structure and function. They have been used for determining the structure of both DNA and RNA in viral, bacterial, and mammalian systems, and also for studying functional questions such as the role of the small nuclear RNAs in processing heteronuclear RNA. A list of some of the major applications of these compounds during the last ten years is presented in Table 1. **Psoralens** are unique in their ability to freeze helical regions of nucleic acid. **Psoralens** react with DNA and RNA by a two-step mechanism. First, the planar **psoralen** molecule intercalates within a double helical region of nucleic acid. Covalent addition of the **psoralen** is effected by controlled irradiation into an absorption band of the **psoralen** molecule. Stable, but photoreversible, covalent adducts form with pyrimidine bases at one or both ends of the **psoralen** molecule. By forming covalent crosslinks with base-paired structures, **psoralens** can probe both static and dynamic structural features. **Psoralens** can trap long-range interactions which are in dynamic equilibrium. This allows both the occurrence of the interaction to be established and its position within the structure to be mapped. **Psoralens** can also be used temporally, such as in following the fate of short-lived nucleic acid species in vivo. The details of the interaction between **psoralens** and nucleic acid are well understood at the molecular level. The structure of the **psoralen** adducts formed with DNA have been determined, the polarity of the reaction which converts monoadduct to crosslink established, and methods for the exclusive formation of monoaddition products developed. This advanced state of chemical control makes the **psoralens** uniquely versatile reagents. As more information is compiled about structure-activity parameters, a fine tuning of the reaction of **psoralens** with nucleic acid will be realized. Future applications of **psoralens** for investigating nucleic acid

structure of nucleic acids will be aided by the following developments. The preparative hybridization probes which carry **psoralen** monoadducts are currently under way. These probes will be used to form covalent adducts for locating particular sequences and also for site-specific placement of **psoralen** monoadducts in nucleic acid structure. The photochemical transfer of the **psoralen**. The transfer of monoadducts will be used for fixation of 'dynamic' base paired intrastructural conformations by crosslink formation. Chemical schemes

for

the site-specific cleavage of DNA and RNA at the position of **psoralen** monoadducts are also being developed. These procedures will allow for the detection of secondary structure at the position of crosslink formation. Finally, many new **psoralen** derivatives are being synthesized for specific applications such as site-directed crosslinking of DNA and protein-nucleic acid crosslinking. **Psoralen** derivatives which will crosslink purine to pyrimidine and purine to purine are also being considered. It is not the intent of this review to catalog the properties and applications of every **psoralen** derivative known. Rather we try to show how a basic understanding of the organic chemistry, photochemistry, and biochemistry of these compounds has produced a versatile molecular tool for the elucidation of nucleic acid structure and function. The use of **psoralens** in the determination of nucleic acid secondary structure is emphasized here. Recent reviews include coverage of other aspects of **psoralens** including clinical applications (1, 2), mutagenesis, toxicity and repair (3), and photochemistry and photophysics (4-6).

L9 ANSWER 3
 ACCESSION NUMBER 83141 0 MEDLINE
 DOCUMENT NUMBER 83141 0 PubMed ID: 6338360
 TITLE: Comparative bacterial **mutagenicity** studies with 8-methoxypsoralen and 4,5',8-trimethyl**psoralen** in the presence of near-ultraviolet light and in the dark.
 AUTHOR: Erikstad D J; Creed K L; Mannisto P
 SOURCE: MUTAGEN RESEARCH, (1983 Feb) 116 (2) 73-82.
 PUBLICATION CODE: NNA; 0400763. ISSN: 0027-5107.
 PUB. COUNTRY: Netherlands
 LANGUAGE: English
 FILE SEGMENT: JOURNAL ARTICLES
 ENTRY MONTH: 1983
 ENTRY DATE: 1983 STN: 19900318
 LAST UPDATED ON STN: 19900318
 INTERC. MEDLINE: 19830415
 AB 2 strains of *Salmonella typhimurium*, TA98 and TA100, and 2 strains of *E. coli*, WP2(pKM101) and WP2uvrA-(pKM101) were used to study **mutagenesis** by 8-methoxypsoralen (8-MOP) and 4,5',8-trimethyl**psoralen** (4,5',8-TMP) in the dark and in the presence of near-ultraviolet (NUV) light both with metabolic activation and with rat-liver S9 at 3 levels (4, 10 and 100 standard cofactors). The S9-independent base substitution **mutagenic** activity of 8-MOP plus NUV light was confirmed with WP2(pKM101), and a similar activity was seen for 4,5',8-TMP, although the substance was active in TA100. The frameshift **mutagenic** activity of 8-MOP in the dark in TA98 was not confirmed despite the high levels which would ensure DNA replication, but this may be due to the low concentrations of 8-MOP achieved in the common solvent system. Both 8-MOP and 4,5',8-TMP were **mutagenic** in WP2uvrA- deficient strains after microsomal activation, and the responses were

similar experiments were conducted in the dark or in NUV light.
 In view of the administration of 8-MOP to psoriasis patients, this finding of relevance in risk assessment, and tends to suggest that topical administration of 4,5',8-TMP to psoriatic patients may present reduced risk of malignant disease.

L9 ANSWER 3 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 ACCESSION NUMBER 209469 EMBASE
 DOCUMENT NUMBER 98207609
 TITLE: Localized **mutagenesis** of the tetracycline promoter region in pBR322 by 4,5',8-trimethylpsoralen.
 AUTHOR: Moon B.
 CORPORATE SOURCE: Cent. Oral Hlth Res., Dept. Anat. Histol., Sch. Dent. Med., Univ. Pennsylvania, Philadelphia, PA 19104, United States
 SOURCE: Mutation Research, (1982) 93/2 (253-262).
 COUNTRY: Netherlands
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 037 Drug Literature Index
 022 Human Genetics
 029 Clinical Biochemistry
 LANGUAGE: English
 AB In vitro mutagenesis of functional DNA gene fragments by covalent linkage permits one in principle to examine the consequences of mutation in DNA sequence directly. I have carried out selective mutagenesis of the tetracycline resistance gene in the plasmid p using the long wavelength UV light activated reaction of 4,5',8-trimethylpsoralen (TMP). The **mutagenized** DNA sequence of the EcoI-Hind III restriction fragment in the vicinity of the Tc.RTM. gene. Two classes of mutants were obtained. One exhibited a high level of resistance (40-60 .mu.g/ml) but still than the wild-type. Interest these showed no sequence alterations at all in the vicinity of the Tc.RTM. gene. The other class of mutants exhibited low levels of resistance (<20 .mu.g/ml) and two of those that were sequenced found to contain a 15-base pair insertion to the right of the Hind III site. Under the conditions used, **psoralen** plus UV treatment appears to be capable of inducing substantial frame-shift mutations in DNA.

L9 ANSWER 3 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 ACCESSION NUMBER 811967 EMBASE
 DOCUMENT NUMBER 19811107
 TITLE: Seedling injury & mitotic aberrations induced by psoralens in barley Hordeum vulgare.
 AUTHOR: Kak S.L.; Kaul B.L.
 CORPORATE SOURCE: Reg. Res. Lab., Jammu 180 001, India
 SOURCE: Indian Journal of Experimental Biology, (1981) 19/7 (643-644).
 COUNTRY: India
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 037 Drug Literature Index
 LANGUAGE: English

L9 ANSWER 3 5 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 ACCESSION NUM: 81141 9 EMBASE
 DOCUMENT NUMB: 198114 589
 TITLE: Photoactions between furocoumarins and DNA: The
 molecular basis of the photochemotherapy of psoriasis.
 AUTHOR: Antonello C.; Baccichetti F.; Bordin F.; et al.
 CORPORATE SOURCE: Inst. Chim. Farmaceut., Univ. Padova, Italy
 SOURCE: Medecine Biologie Environnement, (1980) 8/1 (155-168).
 CODE: MBENDX
 COUNTRY: Belgium
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 037 Drug Literature Index
 LANGUAGE: English

L9 ANSWER 3 5 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 ACCESSION NUM: 80021 1 EMBASE
 DOCUMENT NUMB: 19800 011
 TITLE: Psoralenes in photobiology, applied to
 cosmetology.
 AUTHOR: Forlo P.
 CORPORATE SOURCE: Belgium
 SOURCE: Farmaceutisch Tijdschrift voor België, (1979) 56/3
 (189-198).
 CODE: FMTBB2
 COUNTRY: Belgium
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 037 Drug Literature Index
 LANGUAGE: Dutch

L9 ANSWER 3 5 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 ACCESSION NUM: 78394 0 EMBASE
 DOCUMENT NUMB: 19783 480
 TITLE: Frameshift mutations in bacteria produced in the dark by
 several furocoumarins; Absence of activity of 4,5',8-
 trimethoxypsoralen.
 AUTHOR: Ashwood-Smith M.J.
 CORPORATE SOURCE: Lab. Col. Physico-Chim., Ec. Nat. Superieure Biol. Appl.
 Nutri. Alimentat., Univ. Dijon, France
 SOURCE: Mutation Research, (1978) 58/1 (23-27).
 CODE: MUREAV
 COUNTRY: Netherlands
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 037 Drug Literature Index
 022 Human Genetics
 004 Microbiology
 LANGUAGE: English

AB Four furocoumarins, namely psoralen (P), 8-methoxypsoralen
 (8-MOP), 8-trimethoxypsoralen (TMP) and angelicin (A) were
 tested for mutagenesis in E. coli lac-. Three compounds: P,
 8-MOP and TMP were shown to be weak frameshift mutagens. TMP,
 surprising in view of its very active photosensitizing action, was
 found to be non-mutagenic. These results are discussed in relation to
 the photosensitizing action of the furocoumarins.

=> d history

(FILE 'HIST' ENTERED AT 13:59:16 ON 14 AUG 2001)

```

FILE 'MEDLINE' EMBASE CAPLUS, SCISEARCH, BIOSIS, REGISTRY' ENTERED AT
13:59:35 AUG 01
L1 1598 SORALE?
L2 111 1 AND PSORALEN?
L3 96 2 AND <1998
L4 4 3 AND VERTEBRATE
L5 1 REM L (0 DUPLICATES REMOVED)
L6 2 2 AND ANIMAL
L7 21 6 AND <1998
L8 4 7 AND DIMETHYL?
L9 3 REM L (10 DUPLICATES REMOVED)

=> s 19 and f
L10 0 AND FISH

=> s 19 and ?
5 FILES SELECTED
LEFT TRUNCATION IGNORED FOR FILE 'REGISTRY'
L11 0 AND ?
Left truncation not valid in the specified search field in the
specified file. The term has been searched without left truncation.
Examples: 'TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'

If you are searching in a field that uses implied proximity, and you
used a truncation symbol after a punctuation mark, the system may
interpret the truncation symbol as being at the beginning of a term.
Implied proximity is used in search fields indexed as single words,
for example, 'site index'.

=> s 19 and f
L12 0 AND FISH

=> s 13 and f
L13 0 AND FISH

=> dup rem 11
DUPLICATE IS REMOVED IN 'REGISTRY'.
ANSWERS FROM 11 FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETE FOR 13
L14 1 REM L (0 DUPLICATES REMOVED)

=> d 114 ibib
YOU HAVE REQUESTED 1 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 1 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER 7235 BIOSIS
DOCUMENT NUMBER 799816438
TITLE: Acute myeloid leukemia following psoralen with
ultraviolet A therapy: A fluorescence in situ
hybridization study
AUTHOR(S): Wong, Y. L. (1); Au, W. Y.; Ng, M. H. L.; Chan, L. C.;
Au, W. S.
CORPORATE SOURCE: Department of Pathology, Department of Medicine, Department of
Surgery, Department of Obstetrics and Gynaecology, Department of
Radiology, Department of Pediatrics, Department of Pathology,
Department of Microbiology, Department of Immunology, Department of
Genetics and Cytogenetics, (1997) Vol. 99, No. 1,
pp. 1-13.

```


DOCUMENT TYPE: AB
 LANGUAGE: English
 AB A woman with psoriasis fungoides treated by psoralen with ultraviolet A (PUVA) and electron beam therapy developed acute myeloid leukemia three years later. Karyotypic analysis of the leukemia cells revealed a monoclonal population that had accounted for about a third of the marrow cells after PUVA treatment but replaced the entire marrow at leukemic transformation. These findings were consistent with a secondary AML evolving from an underlying myelodysplasia, supporting that PUVA therapy might have a mutagenic effect on hematopoietic cells. This might be related to its effect on circulating hematopoietic stem cells.

L14 ANSWER 2 MEDLINE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 ACCESSION NUMBER 103443 EMBASE
 DOCUMENT NUMBER 470413
 TITLE: Skin rashes: occurrence, chemistry, biological activity.
 AUTHOR: Lloyda A.
 CORPORATE SOURCE: Peoria Reg. Res. Lab., Peoria, Ill. 61604, United States
 SOURCE: Lloyda, (1975) 38/1 (21-35).
 MODEL: LLOYA2
 DOCUMENT TYPE: Journal
 FILE SEGMENT: 17 Drug Literature Index
 14 Microbiology
 LANGUAGE: English

=> d history

(FILE 'HISTORY' CREATED AT 13:59:16 ON 14 AUG 2001)

FILE 'MEDLINE' SEARCHED, CAPLUS, SCISEARCH, BIOSIS, REGISTRY' ENTERED AT 13:59:35

L1 159
 L2 11 \$
 L3 9
 L4 \$
 L5 \$ (0 DUPLICATES REMOVED)
 L6 2 \$
 L7 2 \$
 L8 2 \$
 L9 10 (10 DUPLICATES REMOVED)
 L10 \$
 L11 \$
 L12 \$
 L13 \$
 L14 \$ (0 DUPLICATES REMOVED)

=> s 16 and 1

L15 \$

=> s 17 and f

L16 \$

=> d l15 ibib

L15 ANSWER 1 BIOSIS COPYRIGHT 2001 BIOSIS
 ACCESSION NUMBER 7: 7235 BIOSIS
 DOCUMENT NUMBER 7 799816438

TITLE: Acute myeloid leukemia following **psoralen** with ultraviolet A therapy: A fluorescence in situ hybridization study

AUTHOR(S): Au, W. Y. L. (1); Au, W. Y.; Ng, M. H. L.; Chan, L. C.; Au, W. Y.

CORPORATE SOURCE: Department of Pathology, Queen Mary Hospital, 113, Yee Hong Rd., Hong Kong Hong Kong

SOURCE: Journal of Clinical Genetics and Cytogenetics, (1997) Vol. 99, No. 1, pp. 13-16. 165-4608.

DOCUMENT TYPE: Article

LANGUAGE: English

AB A woman with ulcerative colitis treated by **psoralen** with ultraviolet A and electron beam therapy developed acute myeloid leukemia 7 years later. Karyotypic analysis of the leukemia cells revealed a normal karyotype. Fluorescence in situ hybridization showed that the monosomy 7 had accounted for about a third of the marrow cells after PUVA therapy but replaced the entire marrow at leukemic transformation. These findings were consistent with a secondary AML arising from pre-existing myelodysplasia, supporting that PUVA therapy might have an adverse effect on hematopoietic cells. This might be related to the direct effect on circulating hematopoietic stem cells.

=> d 116 ibib

L16 ANSWER 1 COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 7235 BIOSIS

DOCUMENT NUMBER: 799816438

TITLE: Acute myeloid leukemia following **psoralen** with ultraviolet A therapy: A fluorescence in situ hybridization study

AUTHOR(S): Au, W. Y. L. (1); Au, W. Y.; Ng, M. H. L.; Chan, L. C.; Au, W. Y.

CORPORATE SOURCE: Department of Pathology, Queen Mary Hospital, 113, Yee Hong Rd., Hong Kong Hong Kong

SOURCE: Journal of Clinical Genetics and Cytogenetics, (1997) Vol. 99, No. 1, pp. 13-16. 165-4608.

DOCUMENT TYPE: Article

LANGUAGE: English

AB A woman with ulcerative colitis treated by **psoralen** with ultraviolet A and electron beam therapy developed acute myeloid leukemia 7 years later. Karyotypic analysis of the leukemia cells revealed a normal karyotype. Fluorescence in situ hybridization showed that the monosomy 7 had accounted for about a third of the marrow cells after PUVA therapy but replaced the entire marrow at leukemic transformation. These findings were consistent with a secondary AML arising from pre-existing myelodysplasia, supporting that PUVA therapy might have an adverse effect on hematopoietic cells. This might be related to the direct effect on circulating hematopoietic stem cells.

=> d history

(FILE 'H0000000000' 13:59:16 ON 14 AUG 2001)

```

FILE 'MEDLINE' CAPLUS, SCISEARCH, BIOSIS, REGISTRY' ENTERED AT
13:59:35 1
L1 1596
L2 113 TAGEN?
L3 96 <1998
L4 4 RTEBRATE
L5 4 (0 DUPLICATES REMOVED)
L6 272 IMAL
L7 213 <1998
L8 4 IMETHYL?
L9 3 (10 DUPLICATES REMOVED)
L10 SH
L11 ISH
L12 SH?
L13 SH?
L14 (0 DUPLICATES REMOVED)
L15 1 SH?
L16 SH?

=> s 13 and py
L17 46 IDINE?

=> s 17 and py
L18 8 IDINE?

=> dup rem 118
DUPLICATE IS N IN 'REGISTRY'.
ANSWERS FROM T LL BE CONSIDERED UNIQUE
PROCESSING COM 3
L19 (2 DUPLICATES REMOVED)

=> d 119 ibib
YOU HAVE REQUESTED 4 6 ANSWERS - CONTINUE? Y/(N):y

L19 ANSWER 1 OF 6
ACCESSION NUMBER 1 MEDLINE
DOCUMENT NUMBER 1 PubMed ID: 8760575
TITLE: Formation of cyclobutane thymine dimers from UVA
sensitization of pyridopsoralen monoadducted DNA.
AUTHOR: L A; Beylot B; Vigny P; Spassky A
CORPORATE SOURCE Instituto de Bioquimica, Universidade de Sao Paulo,
SOURCE: CHEMISTRY AND PHOTOBIOLOGY, (1996 Aug) 64
-55.
code: P69; 0376425. ISSN: 0031-8655.
PUB. COUNTRY: States
Article; (JOURNAL ARTICLE)
LANGUAGE:
FILE SEGMENT: y Journals
ENTRY MONTH:
ENTRY DATE: STN: 19961015
dated on STN: 19961015
Medline: 19961001
AB The present study provides evidence that thymine dimerization can be UVA
photosensitized by a tetranucleotide, 5'-TATT-3', by a
7-methyl-8-hydroxy-2'-deoxyadenosine (7-methyl-8-hydroxy-2'-deoxyadenosine)
of the photoproducts of the tetranucleotide. The efficiency
of the photoproducts depends on the tetranucleotide flanking sequences.
These results indicate that one DNA lesion can originate the
contiguous

```

formation of response to its sensitivity of activity and of DNA in intertype of lesion and emphasize the sequence-specific of drugs with DNA. Results are related to the 1,10-phenanthroline-cuprous ion complex nucleolytic in terms of the major role of local deformability with ligands.

L19 ANSWER 2 OF 6
 MEDLINE
 2
 MEDLINE
 2 PubMed ID: 2342507
 TITLE: Induction of **pyrimidine** cyclobutane dimers for the high cytotoxic effect of 7-methylpyrido[3,4-c]**psoralen** plus UV-A?
 AUTHOR: J. S.
 CORPORATE SOURCE: Institut Curie, Section de Biologie, UA 1292 CNRS, Paris,
 SOURCE: RESEARCH, (1990 May) 235 (3) 203-7.
 code: NNA; 0400763. ISSN: 0027-5107.
 PUB. COUNTRY: France
 LANGUAGE: English
 FILE SEGMENT: Journals
 ENTRY MONTH: May
 ENTRY DATE: STN: 19900720

AB Recently, it was shown that the photoactivation of 7-methylpyrido[3,4-c]**psoralen** (MPP), a highly phototoxic monofunctional compound, as well as leading to the direct cycloaddition of the molecule to **pyrimidine** bases induces the dimerization of adjacent **pyrimidines** in vitro (Moysan et al., 1988). For other **psoralens**, e.g. 8-methoxypsoralen (8-MOP), such a formation of **pyrimidine** dimers does not occur (Costalat et al., 1989). The relatively low level of **pyrimidine** dimers which one can estimate from in vitro results to be formed in vivo in cell DNA after highly lethal photosensitization does not indicate that these dimers have important biological consequences. They could, however, interact with other agents and eventually greatly potentiate their action. In order to test this hypothesis, experiments were designed to mimic the photosensitization by MPP. CV-1 TC-7 cells were irradiated at 254 nm, to produce **pyrimidine** dimers, and subsequently treated with 8-MOP or angelicin plus 365-nm light, to produce **psoralen** adducts. The clonogenicity of these cells was compared to that of cells damaged only by irradiation at 254 nm or by **psoralens** plus 365-nm light. It was observed that, for the same amount of induced adducts, the lethal effect of photosensitization by MPP remains much higher than that of 8-MOP coupled to a large excess of **pyrimidine** dimers induced with 254-nm light. In fact, with both 8-MOP and angelicin, the effects were observed between **pyrimidine** dimers and **psoralen** adducts. (ABSTRACT TRUNCATED AT 200)

L19 ANSWER 3 OF 6
 MEDLINE
 3
 MEDLINE
 3 PubMed ID: 2125562
 TITLE: Biological studies with dioxetanes in isolated DNA, and mammalian cells.
 AUTHOR: Beinbauer A; Mosandl T; Saha-Moller C; Vargas F; Muller E; Schiffmann D; Wild D

CORPORATE SOURCE: Department of Organic Chemistry, University of Wurzburg,
Republic of Germany.

SOURCE: ENVIRONMENTAL HEALTH PERSPECTIVES, (1990 Aug) 88
Ref: 32

code: EIO; 0330411. ISSN: 0091-6765.

PUB. COUNTRY: United States
Article; (JOURNAL ARTICLE)
Review; (REVIEW)
TUTORIAL)

LANGUAGE:

FILE SEGMENT: Journals

ENTRY MONTH:

ENTRY DATE: STN: 19910329

dated on STN: 19910329

Medline: 19910228

AB 1,2-Dioxetanes, potent chemical sources of triplet excited carbonyl compounds, were found to be genotoxic in isolated DNA, bacteria, and cultured mammalian cells. In superhelical DNA of bacteriophage PM2, hydroxyalkyl-substituted dioxetanes (1) induced base-sensitive base modifications and only few single strand breaks. With a specific endonuclease a small fraction of the base modifications identified as **pyrimidine** dimers. The **psoralen** dioxetane, or PsD bound photochemically to calf thymus DNA at the 4-hydroxypyryl ring of **psoralen** (fluorescence measurements). Binding was also observed when calf thymus DNA was incubated with 1 and 3-hydroxymethyl-3,4,4-trimethyl-1,2-dioxetane. In hamster embryo fibroblasts and HL-60 cells, single strand breaks. The alkyl- and hydroxyalkyl-substituted dioxetanes 1 and 2 were efficiently inactivated by cysteine, glutathione, ascorbic acid, tocopherol, NADH and FADH2.

While dioxetanes 1 and 2 were not **mutagenic** in Salmonella typhimurium strain TA100, dioxetanes 3 exhibited substantial effects. Further data indicate that a presumably a **mutagenic** intermediate with a lifetime of minutes is produced from the benzofuran dioxetane.

L19 ANSWER 4 OF 6

NE

DUPLICATE 2

ACCESSION NUMBER: MEDLINE

DOCUMENT NUMBER: PubMed ID: 3115998

TITLE: Repair in specific sequences in mammalian cells.

AUTHOR: A

CORPORATE SOURCE: Department of Biological Sciences, Stanford University, CA 94305.

SOURCE: JOURNAL OF CELL SCIENCE. SUPPLEMENT, (1987) 6

code: HNG; 8502898. ISSN: 0269-3518.

PUB. COUNTRY: United Kingdom
Article; (JOURNAL ARTICLE)

LANGUAGE:

FILE SEGMENT: Journals

ENTRY MONTH:

ENTRY DATE: STN: 19900305

dated on STN: 19900305

Medline: 19871120

AB To investigate the influence of function or activity of a DNA sequence on its repair, we studied excision repair of a number of adducts in the non-transcribed chromatin of alpha DNA of monkey cells (by physically isolating the DNA) also the removal of **pyrimidine** dimers in a number of germline and human cells (by an indirect assay using a

Removal

damage

L19 ANSWER 5 OF 6

COPYRIGHT 2001 ELSEVIER SCI. B.V.

EMBASE

73

AUTHOR:

CORPORATE SOURCE:

SOURCE:

COUNTRY:

FILE SEGMENT:

AB Psoralens comp:

reagents for the investigation of nucleic acid structure and function. They have been used in determining the structure of both DNA and RNA in viral, bacterial, and mammalian systems, and also for studying functional questions, such as the role of the small nuclear RNAs in processing of heteronuclear RNA. At least some of the major applications of these compounds during the last ten years is presented in Table 1. Psoralens are known for their ability to freeze helical regions of nucleic acid. They react with DNA and RNA by a two-step

Article; (JOURNAL ARTICLE)
 LANGUAGE:
 FILE SEGMENT: Journals
 ENTRY MONTH:
 ENTRY DATE: STN: 19900320

Medline: 19841025
 AB Studies of the repair of DNA lesions at biologically important doses is extremely difficult. The most **mutagens**. With 8-methoxypsoralen (8-MOP) and ultraviolet light (UVA) as the lesion-inducing agent, however, it is easy to manipulate the relative frequency of different DNA lesions by means of a special experimental protocol (the tap-and-test procedure) and this can be used to measure repair of DNA adducts. The majority of photoadducts are produced by 8-MOP plus UVA treatment: 8-MOP-DNA monoadducts, 4',5'-cyclobutane monoadducts, and 8-MOP-DNA crosslinks. A monoadduct is formed when a photoactive molecule reacts with a **pyrimidine** base. An 8-MOP-DNA crosslink is formed when an existing monoadduct is photoactivated with another **pyrimidine** base on the opposite strand. Thus monoadducts are formed by absorption of one photon of UVA and crosslinks by absorption of two. In the tap-and-test experiments, cells are exposed to UVA in the presence of 8-MOP and then re-exposed to UVA in the absence of free 8-MOP so that only crosslinks can be produced by UVA treatment. By means of this technique we have previously shown that DNA crosslinks are much more effective than monoadducts in causing chromosomal damage (sister-chromatid exchanges and micronucleus formation) and mutations (Liu-Lee et al., 1984). If L5178Y mouse lymphoma cells are exposed to remove monoadducts, incubation prior to the second UVA treatment should lead to decreases in the effect of re-irradiation. Fewer monoadducts would be available for crosslink formation. We have found that **psoralen** monoadducts are repaired in cells and that about 70% of those capable of crosslink formation are removed or otherwise made unavailable for crosslink formation within 6 h.

=> d history

(FILE 'HOM' 13:59:16 ON 14 AUG 2001)

FILE 'MED' CAPLUS, SCISEARCH, BIOSIS, REGISTRY' ENTERED AT 13:59:35

L1 1590
 L2 113 AGEN?
 L3 960 1998
 L4 42 FEBRATE
 L5 42 (0 DUPLICATES REMOVED)
 L6 270 MAL
 L7 210 1998
 L8 4 METHYL?
 L9 3 (0 DUPLICATES REMOVED)
 L10
 L11 SH
 L12 ?
 L13 ?
 L14 (0 DUPLICATES REMOVED)

L15 1 1? 1?
 L16 1 1? 1?
 L17 40 1? 1?
 L18 8 1? 1?
 L19 6 1? 1? (2 DUPLICATES REMOVED)

=>

---Logging off

=>

Executing the 1

=> LOG Y

COST IN U.S. DC	SINCE FILE	TOTAL
FULL ESTIMATED	ENTRY	SESSION
	223.16	223.31
DISCOUNT AMOUNT	SINCE FILE	TOTAL
CA SUBSCRIBER F	ENTRY	SESSION
	-5.88	-5.88
STN INTERNATIONAL	14:17:29 ON 14 AUG 2001	